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L56  ANSWER 1 OF 48  HCAPLUS  COPYRIGHT 2002 ACS
AN   2002:450196  HCAPLUS
DN   137:19404
TI   Hematopoietic stem cell gene therapy in combination of
     disrupting sex steroid signaling to the thymus for the treatment of T cell
     disorders
IN   Boyd, Richard
PA   Australia
SO   U.S. Pat. Appl. Publ., 51 pp., Cont.-in-part of U. S. Ser. No. 758,910.
     CODEN: USXXCO
DT   Patent
LA   English
IC   C12N015-87; A61K048-00
NCL  424093210
CC   15-8 (Immunochemistry)
     Section cross-reference(s): 1, 2, 14, 63
FAN.CNT 10
     PATENT NO.         KIND  DATE          APPLICATION NO.  DATE
     ---------------    ----  --------      ---------------  --------
PI   US 2002071833      A1    20020613      US 2001-966576   20010926
     WO 2000062657      A2    20001026      WO 2000-AU329    20000417
     WO 2000062657      A3    20010111
          W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
              CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
              ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
              LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
              SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
          RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ,
              MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,
              IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML,
              MR, NE, SN, TD, TG
     EP 1191975         A2    20020403      EP 2000-916705   20000417
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
BR 2000009712 A 20020430 BR 2000-9712 20000417
WO 2002031110 A2 20020418 WO 2001-IB2739 20011012
WO 2002031110 A3 20020620
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2002086001 A1 20020704 US 2001-976599 20011012
US 2002086002 A1 20020704 US 2001-976712 20011012
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US 2000-795302 A2 20001013
US 2001-758910 A2 20010110
US 2001-966576 A 20010926
US 2001-969510 A 20011001

AB The present invention provides methods for gene therapy utilizing hematopoietic **stem cells**, lymphoid **progenitor cells**, and/or myeloid **progenitor cells**. The cells are genetically modified to provide a gene that is expressed in these cells and their progeny after differentiation. In a preferred embodiment the cells contain a gene or gene fragment that confers to the cells resistance to HIV infection and/or replication. The cells are administered to a patient in conjunction with treatment to reactivate the patient's thymus involving disrupting sex steroid signaling to the thymus. The impact of castration on thymic structure and T cell prodn. is investigated in mouse models of immunodepletion. In both **sublethally** irradiated and cyclophosphamide treated mice, castration markedly **enhanced** thymic regeneration. The introduced cells may be autologous, syngeneic, **allogeneic** or xenogeneic, as **tolerance** to foreign cells is created in the patient during reactivation of the thymus. In a preferred embodiment the hematopoietic **stem cells** are CD34+. The patient's thymus is reactivated by disruption of sex steroid mediated signaling to the thymus. In a preferred embodiment, this disruption is created by administration of LHRH agonists, LHRH antagonists, anti-LHRH receptor antibodies, anti-LHRH vaccines or combinations thereof.

ST hematopoietic **stem cell** gene therapy HIV infection; LHRH agonist antagonist vaccine T cell disorder treatment; sex steroid signaling disruption castration T CELL disorder treatment; T cell disorder treatment castration thymic regeneration gene therapy

IT T cell (lymphocyte)
(CD45.2+, remaining high in bone marrow in castrated mice; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT Cell proliferation
(T cell, disease; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT T cell (lymphocyte)
(activation, CD25+CD8+, stimulated by HSV1 infection; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT B cell (lymphocyte)
Macrophage
(anal. in peripheral blood of patients treated with LHRH agonists; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)
IT Vaccines
(anti-LHRH; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)
IT Proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiviral, nucleic acids encoding; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)
IT **Transplant and Transplantation**
(**autotransplant**; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)
IT Mouse
(castrated, disease model; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)
IT Nucleic acids
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(catalytic; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)
IT Lymph node
Spleen
(checking after the castration; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)
IT T cell (lymphocyte)
(cytotoxic; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)
IT Lymph node
(dendritic cell, remaining high in castrated mice; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)
IT T cell (lymphocyte)
(depletion; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)
IT Thymus gland
(disease, atrophy, reversal of age-induced; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)
IT T cell (lymphocyte)
(disease; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)
IT AIDS (disease)
Bone marrow
CD8-positive T cell
Castration
Disease models
Gene therapy
Human
Human T-lymphotropic virus

Human herpesvirus 1
Signal transduction, biological
Thymus gland
Transplant and Transplantation
(hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT CD34 (antigen)
Gonadotropin-releasing hormone receptor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT Double stranded RNA
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT Hematopoiesis
Human immunodeficiency virus
Human immunodeficiency virus 1
(infection, resistance to; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT T cell (lymphocyte)
(infection; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT Drug delivery systems
(injections; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT Dendritic cell
(lymph node, remaining high in castrated mice; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT **Hematopoietic precursor cell**
(lymphoid; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT Gene
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(modified, in hemopoietic **stem cells**; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT Antibodies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal, anti-LHRH receptor; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT Dendritic cell
(myeloid, remaining high in castrated mice; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT **Hematopoietic precursor cell**
(myeloid; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT Lymphocyte
(natural killer cell, anal. in peripheral blood of patients treated

with LHRH agonists; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT T cell (lymphocyte)
(natural killer, anal. in peripheral blood of patients treated with LHRH agonists; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT Gene, microbial
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nef, cells stably transfected with; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT Prostate gland
(neoplasm, sex steroid ablation in patients with; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT Development, mammalian postnatal
(post-pubertal; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT Puberty
(post; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT Gene, microbial
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rev, RevM10 (trans-dominant mutant), cells stably transfected with; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT Gene, microbial
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rev, cells stably transfected with; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT Genetic element
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rev-responsive element, cells stably transfected with; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT Aging, animal
Chemotherapy
Radiation
(reversal of thymic atrophy induced by; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT Steroids, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sex, analogs; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT **Cell**
(**stem**, epithelial; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT **Hematopoietic precursor cell**
(stem; hematopoietic **stem cell** gene therapy in

combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT Sex hormones
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(steroidal, analogs; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT Drug delivery systems
(sustained-release, peptide; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT Ribozymes
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(targeted to HIV tat and/or rev genes, cells stably transfected with; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT Gene, microbial
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tat, cells stably transfected with; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT Thymus gland
(thymocyte; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT Infection
(viral, T cell disorder; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT TCR (T cell receptors)
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(v.beta.10, gene expression in activated lymph nodes infected with HSV1; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT 9034-40-6, LHRH
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(agonists and antagonists; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT 435269-00-4, Leucrin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(for sex steroid ablation; hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT 106-60-5, 5-Aminolevulinic acid
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

IT 13311-84-7, Eulexin 53714-56-0, Leuprolide 57773-63-4, Triptorelin 57773-65-6, Deslorelin 57982-77-1, Buserelin 65807-02-5, Goserelin 66866-63-5, Lutrelin 76932-56-4, Nafarelin 140703-49-7, Meterelin 352234-03-8, Histerelin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(hematopoietic **stem cell** gene therapy in combination of disrupting sex steroid signaling to thymus for treatment of T cell disorders)

L56 ANSWER 2 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **2002:446899** HCAPLUS
DN **137:75247**
TI Targeted radiotherapy as an adjunct to hematopoietic **stem cell transplantation** for advanced leukemia
AU Ruffner, Katherine L.
CS Department of Internal Medicine, Division of Hematology-Oncology, Vanderbilt University, Nashville, TN, USA
SO Cancer Biotherapy & Radiopharmaceuticals (2002), 17(2), 129-135
CODEN: CBRAFJ; ISSN: 1084-9785
PB Mary Ann Liebert, Inc.
DT Journal; General Review
LA English
CC 8-0 (Radiation Biochemistry)
AB A review. Currently, hematopoietic **stem cell transplantation** (HSCT) offers the highest chance of cure for most patients with acute leukemia or chronic myelogenous leukemia (CML) beyond chronic phase. Conditioning regimens consisting of high-dose chemotherapy with or without total body irradn. (TBI) followed by HLA-matched related-donor HSCT offer long-term, disease-free survival rates of 45 % to 65 % for patients with acute myeloid leukemia (AML) **transplanted** in first complete remission (CR); and 30 % for AML patients **transplanted** with refractory or relapsed disease. However, both rates of disease relapse and **transplant**-related mortality remain unacceptably high following HSCT using conventional chemotherapy- and TBI-contg. conditioning regimens, and clin. trials examg. increased-intensity conditioning regimens as a means of reducing the risk of relapse have almost uniformly demonstrated increased **transplant**-related mortality. Targeted radiotherapy delivered by radioimmunoconjugates has evolved as a means of selectively directing radiation to leukemic cells and/or surrounding normal **hematopoietic cells** while relatively sparing radiation-sensitive, non-hematopoietic tissues such as liver, lung, and mucous membranes. Theor., such an approach would serve to decrease both relapse rates and **transplant**-related toxicity and mortality, particularly if targeted radiation could be used in place of, rather than in addn. to., TBI. There are three major components of radioimmunoconjugates that directly affect how well they are able to deliver radiation selectively to target tissues: the antigen against which the antibody is directed, the structure of the antibody itself, and the radioisotope. Each of these components may be modified, albeit with varying degrees of difficulty, in order to improve targeting and tolerability of radioimmunotherapy (RIT). Through modification of the various components of previously studied radioimmunoconjugates, the field of RIT for the treatment of leukemia continues to evolve, and the work reported by Buchmann et al in this issue is indicative of this ongoing evolution.
ST review radiotherapy radioimmunotherapy hematopoietic **stem cell transplantation** leukemia; iodine radioimmunoconjugate **CD33** antibody **stem cell transplantation** leukemia review
IT **Transplant** and **Transplantation**
(hematopoietic **stem cell**; targeted radiotherapy as an adjunct to hematopoietic **stem cell transplantation** for advanced leukemia patients)
IT Antitumor agents
(leukemia; targeted radiotherapy as an adjunct to hematopoietic **stem cell transplantation** for advanced leukemia patients)

IT **Hematopoietic precursor cell**
(stem; targeted radiotherapy as an adjunct to hematopoietic **stem cell transplantation** for advanced leukemia patients)
IT Human
Immunoradiotherapy
Leukemia
Radiotherapy
(targeted radiotherapy as an adjunct to hematopoietic **stem cell transplantation** for advanced leukemia patients)
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L56 ANSWER 3 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **2002:438694** HCAPLUS
DN **137:61663**
TI Cell surface antigen and molecular targeting in the treatment of hematologic malignancies
AU Countouriotis, Athena; Moore, Theodore B.; Sakamoto, Kathleen M.
CS Department of Pediatrics, Mattel Children's Hospital at UCLA, Los Angeles, CA, 90095-1752, USA
SO Stem Cells (Miamisburg, OH, United States) (2002), 20(3), 215-229
CODEN: STCEEJ; ISSN: 1066-5099

PB AlphaMed Press
DT Journal; General Review
LA English
CC 15-0 (Immunochemistry)
AB A review. Conventional cytotoxic therapy of hematol. malignancies is often assocd. with significant morbidity. This morbidity is often due to the lack of specificity for **hematopoietic cells**. Therefore, the concept of targeted therapy for patients with hematol. malignancies has received attention for many years. The goal of monoclonal antibody therapy is to target specific cell surface antigens on malignant **hematopoietic cells**, while sparing normal cells and tissues. Currently, monoclonal antibodies are being evaluated for their cytotoxic effects as well as their ability to deliver toxic agents or radiation. Rituximab, a chimeric anti-CD20 antibody, has shown response rates of approx. 50% with minimal toxicity in patients with refractory indolent lymphoma. Campath-1H (anti-CD52) has shown encouraging results in patients previously treated for chronic lymphocytic leukemia, with response rates up to 33%, although with significant toxicity. Anti-**CD33** antibodies are being used to deliver cytotoxic agents, such as calicheamicin to patients with acute myeloid leukemia with response rates up to 30%. In addn., anti-**CD33** and anti-CD45 antibodies have been used to deliver radiation directly to leukemic cells. 131I-labeled anti-CD45 antibodies are being studied in combination with conventional preparative regimens in patients receiving bone marrow **transplantation**. Lastly, the therapeutic agent STI571 (signal transduction inhibitor 571) has demonstrated the capability of targeting specific mol. abnormalities seen in hematol. malignancies. STI571 targets the tyrosine kinase activity of the bcr-abl fusion protein seen in chronic myeloid leukemia. STI571 has induced complete hematol. responses in up to 98% of patients evaluated in clin. trials.
ST review monoclonal antibody Rituximab campath1H mylotarg hematol malignancy; radioimmunoconjugate iodine 131 antiCD45 bone marrow **transplantation** review
IT Human
(cell surface antigen and mol. targeting in treatment of patients with hematol. malignancies)
IT Neoplasm
(hematol.; cell surface antigen and mol. targeting in treatment of patients with hematol. malignancies)
IT Drug targeting
(mol. targeting; cell surface antigen and mol. targeting in treatment of patients with hematol. malignancies)
IT Antibodies
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal; cell surface antigen and mol. targeting in treatment of patients with hematol. malignancies)
IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(surface; cell surface antigen and mol. targeting in treatment of patients with hematol. malignancies)
RE.CNT 106 THERE ARE 106 CITED REFERENCES AVAILABLE FOR THIS RECORD
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AN **2002:418842** HCAPLUS
DN **137:46037**
TI **Tolerance** induction by megadose **hematopoietic progenitor cells**: Expansion of **veto** cells by short-term culture of purified human CD34+ cells
AU Gur, Hilit; Krauthgamer, Rita; Berrebi, Alain; Klein, Tirza; Nagler, Arnon; Tabilio, Antonio; Martelli, Massimo F.; **Reisner, Yair**
CS Department of Immunology, Weizmann Institute of Science, Rehovot, 76100, Israel
SO Blood (2002), 99(11), 4174-4181
CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
CC 15-10 (Immunochemistry)
AB **Stem cell**-dose escalation is one way to overcome immune rejection of incompatible **stem cells**. However, the no. of hematopoietic precursors required for overcoming the immune barrier in recipients pretreated with **sublethal** regimens cannot be attained with the state-of-the-art technol. for **stem cell** mobilization. This issue was addressed by the observation that cells within the human CD34+ population are endowed with **veto** activity. In the current study, we demonstrated that it is possible to harvest about 28- to 80-fold more **veto** cells on culturing of

purified CD34+ cells for 7 to 12 days with an early-acting cytokine mixt. including Flt3-ligand, **stem cell** factor, and thrombopoietin. Anal. of the expanded cells with fluorescence-activated cell-sorter scanning revealed that the predominant phenotype of CD34+ **CD33**- cells used at the initiation of the culture was replaced at the end of the culture by cells expressing early myeloid phenotypes such as CD34+**CD33**+ and CD34-**CD33**+. These maturation events were assocd. with a significant gain in **veto** activity as exemplified by the minimal ratio of **veto** to effector cells at which significant **veto** activity was detected. Thus, whereas purified unexpanded CD34+ cells exhibited **veto** activity at a **veto**-to-effector cell ratio of 0.5, the expanded cells attained an equiv. activity at a ratio of 0.125. The availability of novel sources of **veto** cells such as those in this study might contribute to the realization of immunol. **tolerance** in "**minitransplants**," without any risk of **graft**-vs.-host disease.

ST **stem cell transplantation**
immunotolerance cytokine GVHD immunotherapy

IT **Hematopoietic precursor cell**
Human
Immunotherapy
(cytokines induced **veto** cell expansion in culture and their use in **immunotolerance** during **stem cell transplantation**)

IT **Stem cell** factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cytokines induced **veto** cell expansion in culture and their use in **immunotolerance** during **stem cell transplantation**)

IT Hemopoietins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(flt3 ligand; cytokines induced **veto** cell expansion in culture and their use in **immunotolerance** during **stem cell transplantation**)

IT **Transplant and Transplantation**
(**graft**-vs.-host reaction; cytokines induced **veto** cell expansion in culture and their use in **immunotolerance** during **stem cell transplantation**)

IT 9014-42-0, Thrombopoietin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cytokines induced **veto** cell expansion in culture and their use in **immunotolerance** during **stem cell transplantation**)

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L56 ANSWER 5 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **2001:685585** HCAPLUS
DN **135:355753**
TI Stromal support augments extended long-term ex vivo expansion of hemopoietic **progenitor cells**
AU Kusadasi, N.; Koevoet, J. L. M.; Van Soest, P. L.; Ploemacher, R. E.
CS Institute of Hematology, Erasmus University Rotterdam, Rotterdam, 3015 GE, Neth.
SO Leukemia (2001), 15(9), 1347-1358
CODEN: LEUKED; ISSN: 0887-6924
PB Nature Publishing Group
DT Journal
LA English
CC 13-5 (Mammalian Biochemistry)
Section cross-reference(s): 2
AB Current technol. to numerically expand hemopoietic stem/**progenitor cells** (HSPC) ex vivo within 1 to 2 wk is insufficient to warrant significant gain in reconstitution time following their **transplantation**. In order to more stringently test the parameters

affecting HSPC expansion, the authors followed ex vivo cultures of CD34+-selected umbilical cord blood (UCB) HSPC for up to 10 wk and investigated the effects of stromal support and cytokine addn. The cytokine combinations included Flt3 ligand (FL) + thrombopoietin (TPO), FL + TPO plus **stem cell** factor (SCF) and/or IL6, or SCF + IL6. To identify the HSPC in uncultured and cultured material, the authors detd. the no. of colony-forming cells (CFC), cobblestone area forming cells (CAFC), the NOD/SCID repopulating ability (SRA), and CD34+ subsets by phenotyping. The highest fold-increase obtained for CD34+ and CD34+CD38- cell nos. was, resp., 1197 and 30,937 for stroma-free and 4066 and 117,235 for stroma-supported cultures. In general, CFC generation increased weekly in FL + TPO contg. groups up to week 5 with a 28- to 195-fold expansion whereafter the weekly CFC output stabilized. Stroma support **enhanced** the expansion of CAFC week 6 maximally 11-fold to 89-fold with FL + TPO + IL6. Cultures stimulated with at least FL + TPO gave an estd. 10- to 14-fold expansion of the ability of CD34+ UCB cells to multilineage **engraft** the BM of **sublethally** irradiated NOD/SCID mice at 2 wk of stroma-free and stroma-supported cultures, while at week 5 and later the estd. SRA decreased to low or undetectable levels in all groups. The authors' results show that stroma and FL + TPO but also inclusion of bovine serum albumin, greatly increase the long-term generation of HSPC as measured by in vitro assays and is indispensable for long-term expansion of CD34+CD38-CXCR4+ cells. However, the different surrogate methods to quantify the HSPC (CD34+CD38-, CFC, CAFC week 6 and SRA) show increasing incongruency with increasing culture time, while esp. the phenotypic anal. and the CFC generation greatly overestimate the CAFC and SRA expansion in 10-wk cultures.

ST hemopoietic **progenitor cell** culture bone marrow stroma cytokine

IT Hemopoietins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(Flt3-ligand; cytokines and stromal support augment extended long-term ex vivo expansion of hemopoietic **progenitor cells**)

IT Animal tissue culture
Hematopoietic precursor cell
(cytokines and stromal support augment extended long-term ex vivo expansion of hemopoietic **progenitor cells**)

IT Interleukin 6
Stem cell factor
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cytokines and stromal support augment extended long-term ex vivo expansion of hemopoietic **progenitor cells**)

IT Bone marrow
(stroma; cytokines and stromal support augment extended long-term ex vivo expansion of hemopoietic **progenitor cells**)

IT 9014-42-0, Thrombopoietin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cytokines and stromal support augment extended long-term ex vivo expansion of hemopoietic **progenitor cells**)

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L56 ANSWER 6 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **2001:596767** HCAPLUS
DN **136:198645**
TI Interleukin 3 improves the ex vivo expansion of primitive human cord **blood progenitor cells** and maintains the **engraftment** potential of SCID repopulating cells
AU Rossmanith, T.; Schroder, B.; Bug, G.; Muller, P.; Klenner, T.; Knaus, R.; Hoelzer, D.; Ottmann, O. G.
CS Department of Hematology and Oncology, III University Medical Center Frankfurt, Frankfurt, Germany
SO Stem Cells (Miamisburg, OH, United States) (2001), 19(4), 313-320
CODEN: STCEEJ; ISSN: 1066-5099
PB AlphaMed Press
DT Journal
LA English
CC 15-5 (Immunochemistry)
AB In umbilical cord blood (UCB) **transplantation**, the no. of nucleated cells per kg is a major predictive and crit. factor of

hematopoietic recovery. Thus, ex vivo expansion of hematopoietic UCB progenitors could potentially accelerate **engraftment**. Whereas Flt-3 ligand (FL), **stem cell** factor (SCF), and thrombopoietin (TPO) are considered indispensable, the role of interleukin 3 (IL-3) is still controversial: it has been reported either to support or abrogate the reconstituting ability of **stem cells**. By adding IL-3 we aimed to **enhance** the amplification of early and committed **progenitor cells** without impairing the long-term **engraftment** of **stem cells**. Demonstrating a pos. impact of IL-3 on the proliferation of all progenitor subsets, the amplification of CD34+ UCB cells was increased 20.9-fold .+-. 5.4 (mean .+-. std. error) in serum-free culture with FL, SCF, TPO, and IL-3 as opposed to 9.3-fold .+-. 3.2 without IL-3 after 7 days. If IL-3 was included, primitive long-term culture-initiating cells and committed colony-forming cells were expanded 16.3-fold .+-. 5.5 and 18.1-fold .+-. 2.4, resp., compared to 12.6-fold .+-. 5.6 and 9.1-fold .+-. 2.0 without IL-3. Anal. of cultured CD34+ UCB cells in **sublethally** irradiated nonobese diabetic/severe combined immunodeficient mice confirmed that cultured cells had preserved their repopulating potential. After 6 wk, all mice showed multilineage **engraftment** with their bone marrow contg. an av. of 45% human CD45+ cells of the unmanipulated sample, 43% of cells after culture in the presence of IL-3, and 27% of cells after culture without IL-3. In combination with early acting cytokines, IL-3 therefore improves the ex vivo expansion of UCB stem and **progenitor cells** without impairing their **engraftment** potential.

ST IL3 cord blood **transplantation** Flt3 ligand TPO SCF

IT Hemopoietins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(FLT3 ligand; IL-3 improves ex vivo expansion of primitive human cord **blood progenitor cells** and maintains **engraftment** potential of SCID repopulating cells)

IT Cord blood
Transplant and **Transplantation**
(IL-3 improves ex vivo expansion of primitive human cord **blood progenitor cells** and maintains **engraftment** potential of SCID repopulating cells)

IT Interleukin 3
Stem cell factor
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IL-3 improves ex vivo expansion of primitive human cord **blood progenitor cells** and maintains **engraftment** potential of SCID repopulating cells)

IT 9014-42-0, Thrombopoietin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IL-3 improves ex vivo expansion of primitive human cord **blood progenitor cells** and maintains **engraftment** potential of SCID repopulating cells)

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L56 ANSWER 7 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **2001:562712** HCAPLUS
DN **135:317006**
TI The development of monoclonal antibody therapy in leukemias
AU Syrigos, Konstantinos N.; Pliarchopoulou, Kyriaki; Harrington, Kevin J.
CS Oncology Unit, 3rd Department of Medicine, Athens Medical School, Sotiria General Hospital, Athens, Greece
SO Hybridoma (2001), 20(3), 145-148
CODEN: HYBRDY; ISSN: 0272-457X
PB Mary Ann Liebert, Inc.
DT Journal; General Review
LA English
CC 15-0 (Immunochemistry)
AB A review with refs. Conventional cytotoxic management of leukemia has less than optimal results, while it is assocd. with life-threatening toxic effects due to lack of specificity for **hematopoietic cells**. Therefore, novel therapeutic strategies with monoclonal antibodies (MAbs) are being explored for delivering chemotherapy or radiation directly to malignant cells. Recently, anti-**CD33** antibodies have been engineered to target malignant myeloid and immature normal cells and have been used to deliver cytotoxic agents or radiation to leukemic cells. 131I-labeled anti-CD45 antibodies are used in combination with conventional chemotherapy in leukemic patients receiving marrow **transplantation**. Addnl., the emergence of Rituximab (against CD20) and Campath-1H (against CD52) for chronic lymphocytic leukemia (CLL) has provided encouraging clin. results for the prognosis of this disease. In conclusion, there has been ongoing research indicating that the approach of patients with leukemia through the application of MAbs might be safer and more effective than current treatment. Considering the preliminary data, MAb therapy appears to be a new, promising weapon in the oncologist's armentarium.
ST review antitumor monoclonal antibody immunotherapy leukemia
IT Immunotherapy
(development of monoclonal antibody therapy in humans with leukemias)

IT Antitumor agents
(leukemia; development of monoclonal antibody therapy in humans with leukemias)
IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal; development of monoclonal antibody therapy in humans with leukemias)
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L56 ANSWER 8 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **2001:549792** HCAPLUS
DN **136:198851**
TI **Stem cell transplantation** across major genetic barriers
AU **Reisner, Yair**
CS Department of Immunology, The Weizmann Institute of Science, Rehovot, 76100, Israel
SO Annals of the New York Academy of Sciences (2001), 938(Hematopoietic Stem Cells 2000), 322-327
CODEN: ANYAA9; ISSN: 0077-8923
PB New York Academy of Sciences
DT Journal
LA English
CC 15-10 (Immunochemistry)
AB Megadose haploidentical **transplants**, mismatched at three HLA loci, **engraft** rapidly and durably without induction of **graft**-vs.-host disease (GVHD). In vitro studies suggest that **veto** cells, contained in the population of hematopoietic progenitors, facilitate this favorable outcome. Cytotoxic T cells, not reactive against the recipient but reactive against a third party, are potent **veto** cells and can synergize with the **stem cells** and facilitate **allogeneic** bone marrow **engraftment** without GVHD. Expts. with mice deficient in FasL and Fas, with transfer of FasL gene and with anti-CD8 antibody, suggest that

the **veto** activity assocd. with cytotoxic T lymphocytes (CTLs) requires simultaneous expression of FasL and CD8.

ST **transplantation stem cell** HLA Fas CD28

IT Gene, animal
Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HLA; **stem cell transplantation** across major genetic barriers)

IT T cell (lymphocyte)
(cytotoxic; **stem cell transplantation** across major genetic barriers)

IT **Transplant and Transplantation**
(**graft**-vs.-host reaction; **stem cell transplantation** across major genetic barriers)

IT Alleles
Genetic polymorphism
Transplant and Transplantation
(**stem cell transplantation** across major genetic barriers)

IT CD8 (antigen)
Fas antigen
Fas ligand
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**stem cell transplantation** across major genetic barriers)

IT **Hematopoietic precursor cell**
(stem; **stem cell transplantation** across major genetic barriers)

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L56 ANSWER 9 OF 48 HCAPLUS

AN **2001:504194** HCAPLUS
TI **Veto** cells effective in preventing **graft rejection** and devoid of **graft** versus host potential
IN **Reisner, Yair**; Martelli, Massimo
PA Yeda Research and Development Co. Ltd., Israel
SO PCT Int. Appl.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001049243	A2	20010712	WO 2000-IL872	20001228
	WO 2001049243	A3	20020131		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	EP 1244803	A2	20021002	EP 2000-983473	20001228

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI	US 2000-477737	A	20000105
	WO 2000-IL872	W	20001228

AB A method of **transplanting** a **transplant** derived from a donor into a recipient is disclosed. The method comprises the steps of (a) **transplanting** the **transplant** into the recipient; and (b) administering to the recipient a dose including non-alloreactive anti-third party cytotoxic T-lymphocytes (CTLs), wherein the non-alloreactive anti-third party CTLs are generated by directing T-lymphocytes of the donor against a third party antigen or antigens, the dose is substantially depleted of T-lymphocytes capable of developing into alloreactive CTLs, thereby preventing or ameliorating both **graft rejection** by the recipient and **graft** versus host disease.

L56 ANSWER 10 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **2001:116382** HCAPLUS
DN **135:225593**
TI Negative influence of IL3 on the expansion of human cord blood in vivo long-term repopulating **stem cells**
AU Piacibello, Wanda; Gammaitoni, Loretta; Bruno, Stefania; Gunetti, Monica; Fagioli, Franca; Cavalloni, Giuliana; Aglietta, M.
CS Department of Biomedical Sciences and Human Oncology, Division of Clinical Oncology, The Institute for Cancer Research and Treatment (IRCC), Candiolo, Italy
SO Journal of Hematotherapy & Stem Cell Research (2000), 9(6), 945-956
CODEN: JHERFM; ISSN: 1525-8165
PB Mary Ann Liebert, Inc.
DT Journal
LA English
CC 15-5 (Immunochemistry)
AB Identification of culture conditions that support expansion or even long-term maintenance of in vivo repopulating human hematopoietic **stem cells** is still a major challenge. Using a combination of FLT3 ligand (FL), **Stem Cell** Factor (SCF), Thrombopoietin (TPO) and Interleukin 6 (IL6), we cultured cord blood (CB) CD34+ cells for up to 12 wk and **transplanted** their

progeny into **sublethally** irradiated NOD/SCID mice. Bone marrow **engraftment** was considered successful when recipients contained measurable nos. of human CD45+, CD71+ and Glycophorin-A+ (GpA) cells 8 wk after **transplantation**. Twelve-week expanded cells with FL+SCF+TPO+IL6 successfully **engrafted** all of the recipients and human CD45++CD71++GpA+ cells represented 4.3 to 22.4% of bone marrow. Substitution of IL6 with IL3 led to an even better expansion of cells and a similar clonogenic progenitor output in the first 8 wk of culture; however, LTC-IC output increased up to week 6 and then decreased and disappeared. By contrast, with FL+SCF+TPO+IL6, LTC-IC kept increasing up to week 12. Four-week cultured cells with FL+SCF+TPO+IL3 less efficiently **engrafted** NOD/SCID mice, both as measured by frequency of pos. recipients (4 out of 10) and percentage of **engrafted** human cells (.ltoreq.2%). Six-week expanded cells failed to **engraft**. This study provides evidence that many, but not all, of the so-called "early acting" cytokines, can sustain long-term maintenance and even expansion of human primitive in vivo repopulating **stem cells**. In particular, in the culture conditions used in this study, the presence of IL3 greatly reduces the repopulating potential of expanded CD34+ CB cells.

ST Interleukin growth factor **stem cell** culture

IT Animal tissue culture
Cord blood
(IL3 in expansion of human cord blood in vivo long-term repopulating **stem cells**)

IT Interleukin 3
Interleukin 6
Stem cell factor
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(IL3 in expansion of human cord blood in vivo long-term repopulating **stem cells**)

IT Hemopoietins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(flt3 ligand; IL3 in expansion of human cord blood in vivo long-term repopulating **stem cells**)

IT **Hematopoietic precursor cell**
(stem; IL3 in expansion of human cord blood in vivo long-term repopulating **stem cells**)

IT 9014-42-0, Thrombopoietin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(IL3 in expansion of human cord blood in vivo long-term repopulating **stem cells**)

RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L56 ANSWER 11 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:885275 HCAPLUS
DN 135:60005
TI Opposing roles of interferon-.gamma. on CD4+ T cell-mediated **graft**-**versus**-host disease: effects of conditioning
AU Welniak, Lisbeth A.; Blazar, Bruce R.; Anver, Miriam R.; Wiltrout, Robert H.; Murphy, William J.
CS Laboratory of Leukocyte Biology and Division of Basic Sciences, SAIC Frederick, NCI-FCRDC, Frederick, MD, 21702-1201, USA
SO Biology of Blood and Marrow Transplantation (2000), 6(6), 604-612
CODEN: BBMTF6; ISSN: 1083-8791
PB Carden Jennings Publishing
DT Journal
LA English
CC 15-8 (Immunochemistry)
AB Although alloreactive T cells are required for the induction of **graft**-vs.-host disease (GVHD), other factors can influence outcome in murine models of the disease. **Lethal** total body irradn. (TBI) conditioning regimens followed by reconstitution with **allogeneic** lymphohematopoietic cells results in the generation of donor anti-host cytotoxic T lymphocyte (CTL)-mediated solid organ (gut, liver, skin) destruction. In contrast, donor anti-host CTL-mediated hematopoietic failure is the primary cause of morbidity following **sublethal** TBI. To det. the role of interferon (IFN)-.gamma. in **graft**-vs.-host reactions against hematopoietic and solid organ targets, we used IFN-.gamma. knockout mice as donors in both **lethal** TBI and bone marrow **transplantation** (BMT) rescue

and **sublethal** TBI models. In this report, we show that CD4+T cells from IFN-.gamma. knockout (KO) mice resulted in accelerated GVHD after **lethal** TBI/BMT using a single major histocompatibility class II mismatch model. In marked contrast, the use of these same IFN-.gamma. KO CD4+ donor cells in combination with **sublethal** TBI significantly ameliorated GVHD-assocd. mortality. In these recipients, severe anemia, bone marrow aplasia, and intestinal lesions were obsd. in the presence but not the absence of donor-derived IFN-.gamma.. Administration of anti-IFN-.gamma. antibodies to **sublethally** irradiated recipients of wild-type donor cells confirmed the role of IFN-.gamma. depletion in CD4+ T cell-mediated GVHD. In conclusion, the extent of conditioning markedly affects the role of IFN-.gamma. in GVHD lesions mediated by CD4+ T cells. In models using **sublethal** TBI, the absence of IFN-.gamma. is protective from GVHD, whereas in **lethal** TBI situations, the loss is deleterious.

ST interferon CD4 T cell MHCII **graft** vs host disease

IT Histocompatibility antigens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(MHC (major histocompatibility complex), class II; interferon-.gamma. effects on conditioning and CD4+ T cell-mediated MHC II-assocd. **graft**-vs.-host disease)

IT **Transplant and Transplantation**
(bone marrow; interferon-.gamma. effects on conditioning and CD4+ T cell-mediated **graft**-vs.-host disease in hematopoietic **stem cell transplantation**)

IT **Transplant and Transplantation**
(**graft**-vs.-host reaction; interferon-.gamma. effects on conditioning and CD4+ T cell-mediated **graft**-vs.-host disease in hematopoietic **stem cell transplantation**
)

IT CD4-positive T cell
(interferon-.gamma. effects on conditioning and CD4+ T cell-mediated **graft**-vs.-host disease in hematopoietic **stem cell transplantation**)

IT **Hematopoietic precursor cell**
(stem; interferon-.gamma. effects on conditioning and CD4+ T cell-mediated **graft**-vs.-host disease in hematopoietic **stem cell transplantation**)

IT Bone marrow
(**transplant**; interferon-.gamma. effects on conditioning and CD4+ T cell-mediated **graft**-vs.-host disease in hematopoietic **stem cell transplantation**)

IT Interferons
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(.gamma.; interferon-.gamma. effects on conditioning and CD4+ T cell-mediated **graft**-vs.-host disease in hematopoietic **stem cell transplantation**)

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L56 ANSWER 12 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **2000:779448** HCAPLUS
DN **134:55449**
TI Anti-third party CD8+ CTLs as potent **veto** cells: coexpression of CD8 and FasL is a prerequisite
AU Reich-Zeliger, S.; Zhao, Y.; Krauthgamer, R.; Bachar-Lustig, E.; **Reisner, Y.**
CS The Department of Immunology, Weizmann Institute of Science, Rehovot, 76100, Israel
SO Immunity (2000), 13(4), 507-515
CODEN: IUNIEH; ISSN: 1074-7613
PB Cell Press
DT Journal
LA English
CC 15-10 (Immunochemistry)
AB Several bone marrow cells and lymphocyte subpopulations, known as " **veto** cells," were shown to induce **transplantation tolerance** across major histocompatibility antigens. Recently, it has been suggested that anti-third party CTLs depleted of alloreactivity are endowed with marked **veto** activity and therefore might potentially facilitate bone marrow **allografting** without **graft** vs. host disease (GVHD). The **veto** mechanism is still obscure. While early studies emphasized the role of CD8-mediated apoptosis, more recent evidence indicates a role for Fas-FasL. In the present study the authors show, by using blocking anti-CD8 antibody, by generating CTLs from FasL or perforin mutated mice, and by gene transfer of FasL, that the **veto** activity of anti-third party CD8+ CTLs is dependent upon the simultaneous expression of both CD8 and FasL.
ST cytotoxic T cell **veto** function CD8 Fas ligand
IT CD8-positive T cell
(coexpression of CD8 and Fas ligand is prerequisite for **veto** function of)
IT CD8 (antigen)
Fas ligand
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cytotoxic T-cell coexpression of CD8 and Fas ligand is prerequisite for **veto** function)
IT Fas antigen
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cytotoxic T-cell coexpression of CD8 and Fas ligand is prerequisite for **veto** function)
IT **Immune tolerance**
(cytotoxic T-cell coexpression of CD8 and Fas ligand is prerequisite

for **veto** function in relation to)
IT T cell (lymphocyte)
(cytotoxic, CD8+; coexpression of CD8 and Fas ligand is prerequisite for **veto** function of)
RE.CNT 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L56 ANSWER 13 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **2000:646654** HCAPLUS
DN **133:308710**
TI **Tolerance** induction by "megadose" **transplants** of CD34+ **stem cells**: a new option for leukemia patients without an HLA-matched donor
AU **Reisner, Yair**; Martelli, Massimo F.
CS Department of Immunology, Weizmann Institute of Science, Rehovot, 76100, Israel
SO Current Opinion in Immunology (2000), 12(5), 536-541
CODEN: COPIEL; ISSN: 0952-7915
PB Elsevier Science Ltd.
DT Journal; General Review
LA English
CC 15-0 (Immunochemistry)
AB A review with 47 refs. Early studies in murine models and more recent clin. data in heavily pre-treated leukemia patients have shown that escalation of the dose of **hematopoietic progenitor cells** can overcome major genetic barriers and enable rapid and durable **engraftment** of haploidentical, three-locus-mismatched **transplants** without **graft**-vs.-host disease. In vitro studies suggest that **veto** cells within the progenitor population most probably mediate this facilitating effect.
ST review **tolerance stem cell allograft** leukemia
IT **Transplant and Transplantation**
(**allotransplant**; mol. mechanisms of **allograft tolerance** to CD34+ **stem cells** in leukemia therapy)
IT Adoptive immunotherapy
Immune tolerance
Leukemia
(mol. mechanisms of **allograft tolerance** to CD34+ **stem cells** in leukemia therapy)
IT **Hematopoietic precursor cell**
(stem; mol. mechanisms of **allograft tolerance** to CD34+ **stem cells** in leukemia therapy)
RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L56 ANSWER 14 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **2000:554488** HCAPLUS
DN **134:235941**
TI Increases in autologous hematopoietic progenitors in the blood of baboons following irradiation and treatment with porcine **stem cell** factor and interleukin-3
AU Down, J. D.; Awwad, M.; Kurilla-Mahon, B.; Moran, K.; Ericsson, T.; Oldmixon, B.; Lachance, A.; Watts, A.; Treter, S.; Nash, K.; Gojo, S.; Sachs, D. H.; White-Scharf, M. E.; Cooper, D. K. C.
CS BioTransplant Inc., Charleston, MA, USA
SO Transplantation Proceedings (2000), 32(5), 1045-1046
CODEN: TRPPA8; ISSN: 0041-1345
PB Elsevier Science Inc.
DT Journal
LA English
CC 15-5 (Immunochemistry)
AB A study was conducted to investigate the effect of administering porcine cytokines on **sublethally** irradiated baboons **transplanted** with mobilized pig peripheral blood mononuclear cells with respect to the content of circulating hematopoietic progenitors. Results confirm that porcine cytokine **stem cell** factor (pSCF) is cross-reactive with primate cells and demonstrate that it induces a mobilizing effect on hematopoietic progenitors in the blood after irradn. This cross-reactive effect should be considered in attempts to use porcine cytokines to promote a pig **stem cell engraftment** during xenogeneic **transplantation**.
ST hematopoietic progenitor **stem cell** factor IL3 **xenotransplantation**
IT **Hematopoietic precursor cell**
Mononuclear cell (leukocyte)
Swine
(increases in autologous hematopoietic progenitors in blood of baboons following irradn. and treatment with porcine **stem cell** factor and interleukin-3)
IT Interleukin 3
Stem cell factor

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(increases in autologous hematopoietic progenitors in blood of baboons following irradn. and treatment with porcine **stem cell** factor and interleukin-3)
IT **Transplant** and **Transplantation**
(**xenotransplant**; increases in autologous hematopoietic progenitors in blood of baboons following irradn. and treatment with porcine **stem cell** factor and interleukin-3)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L56 ANSWER 15 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **2000:467709** HCAPLUS
DN **134:191840**
TI Targeted therapy of acute myeloid leukemia with monoclonal antibodies and immunoconjugates
AU Sievers, Eric L.
CS Department of Pediatrics, Fred Hutchinson Cancer Research Center, Clinical Research Division, University of Washington, Seattle, WA, 98109-1024, USA
SO Cancer Chemotherapy and Pharmacology (2000), 46(Suppl.), S18-S22
CODEN: CCPHDZ; ISSN: 0344-5704
PB Springer-Verlag
DT Journal; General Review
LA English
CC 15-0 (Immunochemistry)
Section cross-reference(s): 1
AB A review with 24 refs. Traditional chemotherapy for acute leukemia often causes life-threatening toxic effects due to a lack of specificity for **hematopoietic cells**. Monoclonal antibodies and fusion proteins that target cell surface antigens on leukemic blasts are being evaluated for their cytotoxic effects and as a means of delivering chemotherapeutic agents or radiation directly to malignant cells. It is hoped that this strategy might selectively ablate malignant cells without many of the toxic effects commonly assocd. with conventional chemotherapy. In acute myeloid leukemia (AML), the cell surface antigens **CD33** and CD45 are esp. suitable targets. Although **CD33** is expressed on AML blast cells from about 90% of patients, normal hematopoietic **stem cells** lack it, as do essentially all nonhematopoietic tissues. For that reason, anti-**CD33** antibodies have been created to target malignant myeloid and immature normal cells selectively while sparing normal **stem cells**. Anti-**CD33** antibodies have also been used to deliver radiation or a cytotoxic agent directly to leukemic cells. Since the vast majority of leukemias and normal **stem cells** express the cell surface antigen CD45, another targeting approach allows the delivery of myeloablative radiation to bone marrow and spleen, common sites of leukemic involvement. Consequently, 131I-labeled anti-CD45 antibody has been combined with traditional preparative regimens for patients receiving bone marrow **transplantation** for acute leukemia. Finally, fusion proteins such as those combining diphtheria toxin with granulocyte-macrophage colony-stimulating factor (GM-CSF) to target the GM-CSF receptor are now being evaluated in clin. trials. Both unconjugated and conjugated antibodies have shown promise in early clin. trials, and may represent appealing therapeutic alternatives for patients with AML.
ST acute myeloid leukemia antitumor monoclonal antibody immunoconjugate review
IT CD antigens
RL: BOC (Biological occurrence); BSU (Biological study, unclassified);

BIOL (Biological study); OCCU (Occurrence)
(**CD33**, monoclonal antibodies to; targeted therapy of acute myeloid leukemia with monoclonal antibodies and immunoconjugates)
IT Antitumor agents
(acute myelogenous leukemia; targeted therapy of acute myeloid leukemia with monoclonal antibodies and immunoconjugates)
IT Drug delivery systems
(immunoconjugates; targeted therapy of acute myeloid leukemia with monoclonal antibodies and immunoconjugates)
IT Drug delivery systems
(immunotoxins; targeted therapy of acute myeloid leukemia with monoclonal antibodies and immunoconjugates)
IT CD45 (antigen)
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(monoclonal antibodies to; targeted therapy of acute myeloid leukemia with monoclonal antibodies and immunoconjugates)
IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal; targeted therapy of acute myeloid leukemia with monoclonal antibodies and immunoconjugates)
IT Fusion proteins (chimeric proteins)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(targeted therapy of acute myeloid leukemia with monoclonal antibodies and immunoconjugates)
IT 83869-56-1, GM-CSF
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fusion protein with diphtheria toxin; targeted therapy of acute myeloid leukemia with monoclonal antibodies and immunoconjugates)
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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L56 ANSWER 16 OF 48 HCAPLUS

AN **2000:456687** HCAPLUS
DN **133:69437**
TI Human growth hormone to stimulate mobilization of pluripotent hematopoietic **stem cells**
IN Gianni, Allesandro Massimo
PA Applied Research Systems ARS Holding N.V., Neth. Antilles
SO Eur. Pat. Appl., 24 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM A61K038-27
ICS C12N005-06; C12N005-08; A61K035-14; A61K035-28
ICI A61K038-27, A61K038-19
CC 2-5 (Mammalian Hormones)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1016413	A1	20000705	EP 1998-124834	19981230
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	WO 2000040260	A1	20000713	WO 1999-EP10470	19991230
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	BR 9916726	A	20010911	BR 1999-16726	19991230
	EP 1140149	A1	20011010	EP 1999-965579	19991230
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002534393	T2	20021015	JP 2000-592015	19991230
PRAI	EP 1998-124834	A	19981230		
	WO 1999-EP10470	W	19991230		

AB A method is claimed for the prepn. of a population of circulating cells capable of regenerating hematopoiesis in vivo comprising: (a) administering to a donor a compn. comprising growth hormone or one of its derivs. or any factor inducing growth hormone release in an amt. sufficient to increase in said donor the no. of circulating cells capable of regenerating hematopoiesis in vivo and (b) isolating a population of circulating cells capable of regenerating hematopoiesis in vivo from the peripheral blood of said donor. A method is claimed for prepn. of a population of circulating cells capable of regenerating hematopoiesis in vivo comprising: (a) administering to a donor a compn. comprising growth hormone or one of its derivs. or any factor inducing growth hormone release in an amt. sufficient to reduce the vol. of blood required to be processed in order to obtain the specified target no. of circulating cells capable of regenerating hematopoiesis in vivo, (b) isolating said reduced vol. of blood and (c) isolating a population of circulating cells capable of regenerating hematopoiesis in vivo from said isolated vol. The compns. of the invention can also comprise one or more of the following groups of compds.: hematopoietic growth factors, cytokines, chemokines, monoclonal antibodies. Also claimed is the use of human growth hormone or one of its derivs. or any factor inducing human growth hormone release to prep. a medicament for **enhancing** hematopoietic reconstitution. The medicaments of the invention can be used to treat a neoplastic disease, a hematol. disorder, malignancies, severe combined immune deficiencies, hematopoietic abnormalities, anemia, aplastic anemia, leukemia and/or osteopetrosis. They can also be used to reduce the bone marrow aplasia period which follows **transplantation**, for preventing and/or

treating opportunistic infections after **transplantation** or for limiting the risk of tumor recurrence after **transplantation**. As well, they can be used for preventing and/or treating secondary effects of myelosuppressive therapy and/or radiotherapy and/or chemotherapy. The medicament comprises further one or several compds. chosen among the following: hematopoietic growth factors, cytokines, chemokines, monoclonal antibodies. A method is also claimed for the **enhancement** of hematopoiesis reconstitution comprising the steps of: (a) administering to a donor a compn. comprising growth hormone or one of its derivs. or any factor inducing growth hormone release in an amt. sufficient to increase in said donor the no. of circulating cells capable of regenerating hematopoiesis in vivo, (b) isolating a population of circulating cells capable of regenerating hematopoiesis in vivo from the peripheral blood of said donor, (c) **transplantation** of the cells recovered in step (b) to an individual, and (d) administration of growth hormone in an amt. sufficient to accelerate hematopoietic recovery.

ST growth hormone hematopoietic **stem cell** mobilization

IT CD antigens
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**CD33**, CD34+/**CD33**+ or **CD33**+ cells; human growth hormone to stimulate mobilization of pluripotent hematopoietic **stem cells**)

IT CD34 (antigen)
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(CD34+ cells; human growth hormone to stimulate mobilization of pluripotent hematopoietic **stem cells**)

IT CD38 (antigen)
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(CD34+/Thy-1/CD38- cells; human growth hormone to stimulate mobilization of pluripotent hematopoietic **stem cells**)

IT Antigens
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(Thy-1, CD34+/Thy-1 cells and/or CD34+/Thy-1/CD38- cells; human growth hormone to stimulate mobilization of pluripotent hematopoietic **stem cells**)

IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-VLA-4; compns. contg. human growth hormone and other components to stimulate mobilization of pluripotent hematopoietic **stem cells**)

IT **Transplant** and **Transplantation**
Transplant and **Transplantation**
(bone marrow; compns. contg. human growth hormone and other components to stimulate mobilization of pluripotent hematopoietic **stem cells**)

IT Antitumor agents
(compns. contg. human growth hormone and other components to stimulate mobilization of pluripotent hematopoietic **stem cells**)

IT Chemokines
Cytokines
Hemopoietins
Interleukin 1
Interleukin 3
Macrophage inflammatory protein 1.alpha.
Stem cell factor

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. contg. human growth hormone and other components to stimulate mobilization of pluripotent hematopoietic **stem cells**
)

IT Blood
(disease, treatment; compns. contg. human growth hormone and other components to stimulate mobilization of pluripotent hematopoietic **stem cells**)

IT Cell migration
Hematopoiesis
(human growth hormone to stimulate mobilization of pluripotent hematopoietic **stem cells**)

IT Plasmapheresis
(leukapheresis; human growth hormone to stimulate mobilization of pluripotent hematopoietic **stem cells**)

IT Antitumor agents
(leukemia; compns. contg. human growth hormone and other components to stimulate mobilization of pluripotent hematopoietic **stem cells**)

IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal; compns. contg. human growth hormone and other components to stimulate mobilization of pluripotent hematopoietic **stem cells**)

IT Agranulocytosis
(neutropenia, treatment; compns. contg. human growth hormone and other components to stimulate mobilization of pluripotent hematopoietic **stem cells**)

IT Bone, disease
(osteopetrosis, treatment; compns. contg. human growth hormone and other components to stimulate mobilization of pluripotent hematopoietic **stem cells**)

IT **Transplant** and **Transplantation**
(peripheral blood **stem cells**; human growth hormone to stimulate mobilization of pluripotent hematopoietic **stem cells**)

IT Immunodeficiency
(severe combined, treatment; compns. contg. human growth hormone and other components to stimulate mobilization of pluripotent hematopoietic **stem cells**)

IT **Hematopoietic precursor cell**
(stem; human growth hormone to stimulate mobilization of pluripotent hematopoietic **stem cells**)

IT Platelet (blood)
(thrombocytopenia, treatment; compns. contg. human growth hormone and other components to stimulate mobilization of pluripotent hematopoietic **stem cells**)

IT Bone marrow
Bone marrow
(**transplant**; compns. contg. human growth hormone and other components to stimulate mobilization of pluripotent hematopoietic **stem cells**)

IT Chemotherapy
Radiotherapy
(treatment of side effects from; compns. contg. human growth hormone and other components to stimulate mobilization of pluripotent hematopoietic **stem cells**)

IT Anemia (disease)
Hemorrhage

(treatment; compns. contg. human growth hormone and other components to stimulate mobilization of pluripotent hematopoietic **stem cells**)

IT Integrins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.alpha.4.beta.1; compns. contg. human growth hormone and other components to stimulate mobilization of pluripotent hematopoietic **stem cells**)

IT 9014-42-0, Thrombopoietin 83869-56-1, GM-CSF 143011-72-7, G-CSF
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. contg. human growth hormone and other components to stimulate mobilization of pluripotent hematopoietic **stem cells**)

IT 9002-72-6, Somatotropin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human growth hormone to stimulate mobilization of pluripotent hematopoietic **stem cells**)

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L56 ANSWER 17 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:324019 HCAPLUS
TI Adoptive immunotherapy in canine mixed chimeras after nonmyeloablative **hematopoietic cell transplantation**
AU Georges, George E.; Storb, Rainer; Thompson, Jennifer D.; Yu, Cong; Gooley, Ted; Bruno, Benedetto; Nash, Richard A.
CS Clinical Research Division, Fred Hutchinson Cancer Research Center, Department of Medicine, University of Washington, Seattle, WA, USA
SO Blood (2000), 95(10), 3262-3269
CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB Development of nontoxic and nonmyeloablative regimens for **allogeneic** hematopoletic **stem-cell transplantation** will decrease **transplantation**-related mortality caused by regimen-related toxic effects. In pursuit of this goal, a dog model of stable mixed hematopoietic chimerism was established in which leukocyte-antigen-identical litter mates are given **sublethal** total-body irradn. (2 Gy) before **stem-cell transplantation** and immunosuppression with mycophenolate mofetil and cyclosporine afterward. In the current study, we examd. whether donor lymphocyte infusion (DLI) could be used as adoptive immunotherapy to convert mixed to complete donor chimerism. First, 8 mixed chimeras were given unmodified DLI between day 36 and day 414 after **stem-cell transplantation**. After a 10- to 47-wk follow-up period, there were no significant changes in the percentage of donor **engraftment**. Next, we immunized the donor

to the minor histocompatibility antigens (mHA) of the recipient by means of repeated skin **grafting**. Lymphocytes from the mHA-sensitized donor were infused between day 201 and day 651 after **transplantation**. All 8 recipients of mHA-sensitized DLI had conversion to greater than 98% donor chimerism within 2 to 12 wk of the infusion. Complications from mHA-sensitized DLI included **graft** -vs.-host disease in 2 dogs and marrow aplasia in 1. These results showed that the low-dose **transplant** regimen establishes **immune tolerance**, and mHA-sensitized DLI is required to break **tolerance**, thereby converting mixed to complete donor chimerism. We propose that mixed chimerism established after nonmyeloablative **allogeneic stem-cell transplantation** provides a platform for adoptive immunotherapy that has clin. potential in the treatment of patients with malignant diseases.

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L56 ANSWER 18 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:785178 HCAPLUS
DN 132:92262
TI CD8+TCR+ and CD8+TCR- cells in whole bone marrow facilitate the **engraftment** of hematopoietic **stem cells** across **allogeneic** barriers
AU Gandy, Kimberly L.; Domen, Jos; Aguila, Hector; Weissman, Irving L.
CS Department of Pathology and Developmental Biology Stanford University Medical Center, Stanford University, Stanford, CA, 94305, USA
SO Immunity (1999), 11(5), 579-590
CODEN: IUNIEH; ISSN: 1074-7613
PB Cell Press
DT Journal
LA English
CC 15-10 (Immunochemistry)
AB Although purified hematopoietic **stem cells** (HSC) are sufficient to **engraft** irradiated **allogeneic** recipients, bone marrow (BM) contains other cells that facilitate **engraftment**. Here, several candidate facilitators were tested by **cotransplantation** with HSC. Both TCR+ and TCR-CD8.alpha.+ BM subpopulations have facilitative potential. CD8+TCR+ cells are typical T lymphocytes. CD8+TCR- facilitators are CD3-, not CD3+, have a granular morphol., and are CD8.beta.- and CD11c+; they share phenotypic characteristics with CD8.alpha..alpha. lymphoid dendritic cells and **veto** cells. We also demonstrate that lytic function is not necessary for facilitation and that the CD8.alpha. mol. is either important for facilitation or in the development of facilitators.
ST bone marrow **allograft** hematopoietic **stem cell** CD8
IT CD8-positive T cell
Mouse
(CD8+TCR+ and CD8+TCR- cells in whole bone marrow facilitate **engraftment** of hematopoietic **stem cells** across **allogeneic** barriers)
IT **Transplant and Transplantation**
Transplant and Transplantation
(**allotransplant**, bone marrow; CD8+TCR+ and CD8+TCR- cells in whole bone marrow facilitate **engraftment** of hematopoietic **stem cells** across **allogeneic** barriers)
IT Bone marrow
(**allotransplant**; CD8+TCR+ and CD8+TCR- cells in whole bone marrow facilitate **engraftment** of hematopoietic **stem cells** across **allogeneic** barriers)
IT **Hematopoietic precursor cell**
(stem; CD8+TCR+ and CD8+TCR- cells in whole bone marrow facilitate **engraftment** of hematopoietic **stem cells** across **allogeneic** barriers)
IT CD8 (antigen)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.alpha.-chain; CD8+TCR+ and CD8+TCR- cells in whole bone marrow facilitate **engraftment** of hematopoietic **stem cells** across **allogeneic** barriers)
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L56 ANSWER 19 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **1999:710547** HCAPLUS
DN **132:220893**

TI Antibody-targeted therapy for myeloid leukemia
AU Appelbaum, Frederick R.
CS Clinical Research Division, Fred Hutchinson Cancer Research Center, University of Washington School of Medicine, Seattle, WA, USA
SO Seminars in Hematology (1999), 36(4, Suppl. 6), 2-8
CODEN: SEHEA3; ISSN: 0037-1963
PB W. B. Saunders Co.
DT Journal; General Review
LA English
CC 15-0 (Immunochemistry)
Section cross-reference(s): 8
AB A review with 29 refs. The availability of antibodies reactive with antigens expressed only by **hematopoietic cells** has provided clin. investigators with new tools for use in developing therapies for acute myeloid leukemia (AML). Studies performed to date have investigated the use of such antibodies in an unmodified state, combined with potent chems. to form immunotoxins or combined with various radionuclides. Encouraging results have been obtained in all three settings. The **CD33** antigen is expressed by most early myeloid cells and by more than 90% of cases of AML but is not present on the hematopoietic **stem cell**. Initial in vivo studies with an unmodified murine anti-**CD33** antibody in patients with AML demonstrated that the antibody quickly bound to leukemia cells and that the antigen-antibody complex rapidly internalized following cell binding. However, when administered to patients with overt leukemia, unmodified antibody resulted in only brief decreases in peripheral blast counts, not in sustained response. A no. of **CD33**-based immunotoxins have also been studied, including a calicheamicin conjugate, CMA-676. In a phase I dose-escalation study of patients with refractory AML, CMA-676 was well tolerated with the only consistent toxicities being the development of fevers and chills several hours after administration and the subsequent development of temporary pancytopenia. A phase III study has been performed involving patients with AML in first relapse. An interim anal. of the first 23 patients found that in 10, treatment with CMA-676 resulted in elimination of blasts from peripheral blood and marrow. This was achieved with far less toxicity than seen with std. chemotherapy. Radiolabeled antibodies have been explored as a stand-alone treatment or in the context of bone marrow **transplantation**. In an effort to avoid toxicities to normal **stem cells** residing alongside leukemic cells in the marrow, studies have been performed to explore the use of 231Bi conjugated to an anti-**CD33** monoclonal antibody. The short path length of this alpha-emitter could theor. allow killing of the targeted leukemic cell without damage to normal neighbors. Of 12 patients with recurrent AML who received this drug, eight had redns. in marrow and peripheral blast counts. Complete remissions (CRs) have not been obsd. to date. Another set of studies focused on the use of radiolabeled antibodies to deliver radiation specifically to sites of leukemia as part of a **transplant** preparative regimen. In a phase I clin. trial, 131I-labeled anti-CD45 antibody delivered at least threefold more radiotherapy to spleen and marrow than any other organ. In a phase II trial, among 25 AML patients in first remission, 22 are alive and in remission for periods up to 6 yr.
ST review antibody therapy myeloid leukemia
IT Immunoradiotherapy
Immunotherapy
(antibody-targeted therapy for myeloid leukemia)
IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibody-targeted therapy for myeloid leukemia)
IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(labeled; antibody-targeted therapy for myeloid leukemia)
IT Antitumor agents
(myelogenous leukemia; antibody-targeted therapy for myeloid leukemia)
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L56 ANSWER 20 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **1999:700863** HCAPLUS
TI Induction of donor-type chimerism and **transplantation tolerance** across major histocompatibility barriers in **sublethally** irradiated mice by Sca-1+Lin- bone marrow **progenitor cells**: synergism with non-alloreactive (host .times. donor)F1 T cells
AU Bachar-Lustig, Esther; Li, Hong Wei; Gur, Hilit; Krauthgamer, Rita; Marcus, Hadar; **Reisner, Yair**
CS Department of Immunology, Weizmann Institute of Science, Rehovot, 76100, Israel
SO Blood (1999), 94(9), 3212-3221
CODEN: BLOOAW; ISSN: 0006-4971
PB W. B. Saunders Co.
DT Journal
LA English
AB Induction of **transplantation tolerance** by means of bone marrow (BM) **transplantation** could become a reality if it was possible to achieve **engraftment** of hematopoietic **stem cells** under **nonlethal** preparatory cytoredn. of the recipient. To that end, BM facilitating cells, **veto** cells, or other **tolerance**-inducing cells, have been extensively studied. In the present study, we show that BM cells within the Sca-1+Lin- cell fraction, previously shown to be enriched for early hematopoietic progenitors, are capable of reducing specifically antidonor

CTL-p frequency in vitro and in vivo, and of inducing split chimerism in **sublethally** 7-Gy-irradiated recipient mice across major histocompatibility complex barriers. The **immune tolerance** induced by the Sca-1+Lin- cells was also assocd. with specific **tolerance** toward donor-type skin **grafts**. The minimal no. of cells required to overcome the host immunity remaining after 7 Gy total body irradn. is very large and, therefore, it may be very difficult to harvest sufficient cells for patients. This challenge was further addressed in our study by demonstrating that nonalloreactive (host .times. donor)F1 T cells, previously shown to **enhance** T-cell-depleted BM **allografts** in **lethally** irradiated mice, synergize with Sca-1+Lin- cells in their capacity to overcome the major **transplantation** barrier presented by the **sublethal** mouse model.

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L56 ANSWER 21 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **1999:644127** HCAPLUS
DN **131:331903**
TI Efficient and durable gene marking of **hematopoietic progenitor cells** in nonhuman primates after nonablative conditioning
AU Rosenzweig, M.; MacVittie, T. J.; Harper, D.; Hempel, D.; Glickman, R. L.; Johnson, R. P.; Farese, A. M.; Whiting-Theobald, N.; Linton, G. F.; Yamasaki, G.; Jordan, C. T.; Malech, H. L.
CS England Regional Primate Research Center, Harvard Medical School,

Southborough, MA, USA
SO Blood (1999), 94(7), 2271-2286
CODEN: BLOOAW; ISSN: 0006-4971
PB W. B. Saunders Co.
DT Journal
LA English
CC 1-8 (Pharmacology)
AB Optimization of mobilization, harvest, and transduction of hematopoietic **stem cells** is crit. to successful **stem cell** gene therapy. We evaluated the utility of a novel protocol involving Flt3-ligand (Flt3-L) and granulocyte colony-stimulating factor (G-CSF) mobilization of peripheral blood **stem cells** and retrovirus transduction using hematopoietic growth factors to introduce a reporter gene, murine CD24 (mCD24), into hematopoietic **stem cells** in nonhuman primates. Rhesus macaques were treated with Flt3-L (200 .mu.g/kg) and G-CSF (20 .mu.g/kg) for 7 days and autologous CD34+ peripheral blood **stem cells** harvested by leukapheresis. CD34+ cells were transduced with an MFGS-based retrovirus vector encoding mCD24 using 4 daily transductions with centrifugations in the presence of Flt3-L (100 ng/mL), human **stem cell** factor (50 ng/mL), and PIXY321 (50 ng/mL) in serum-free medium. An important and novel feature of this study is that **enhanced** in vivo **engraftment** of transduced **stem cells** was achieved by conditioning the animals with a low-morbidity regimen of **sublethal** irradn. (320 to 400 cGy) on the day of **transplantation**. **Engraftment** was monitored sequentially in the bone marrow and blood using both multiparameter flow cytometry and semi-quant. DNA polymerase chain reaction (PCR). Our data show successful and persistent **engraftment** of transduced primitive progenitors capable of giving rise to marked cells of multiple hematopoietic lineages, including granulocytes, monocytes, and B and T lymphocytes. At 4 to 6 wk **posttransplantation**, 47% .+-. 32% (n = 4) of granulocytes expressed mCD24 antigen at the cell surface. Peak in vivo levels of genetically modified peripheral blood lymphocytes approached 35% .+-. 22% (n = 4) as assessed both by flow cytometry and PCR 6 to 10 wk **posttransplantation**. In addn., naive (CD45RA+ and CD62L+) CD4+ and CD8+ cells were the predominant phenotype of the marked CD3+ T cells detected at early time points. A high level of marking persisted at between 10% and 15% of peripheral blood leukocytes for 4 mo and at lower levels past 6 mo in some animals. A cytotoxic T-lymphocyte response against mCD24 was detected in only 1 animal. This degree of persistent long-lived, high-level gene marking of multiple hematopoietic lineages, including naive T cells, using a nonablative marrow conditioning regimen represents an important step toward the ultimate goal of high-level permanent transduced gene expression in **stem cells**.
ST gene therapy hematopoietic progenitor growth factor
IT Hematopoietin receptors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(FLT3 receptors, ligand; efficient and durable gene marking of **hematopoietic progenitor cells** in nonhuman primates after nonablative conditioning)
IT **Transplant** and **Transplantation**
Transplant and **Transplantation**
(bone marrow; efficient and durable gene marking of **hematopoietic progenitor cells** in nonhuman primates after nonablative conditioning)
IT T cell (lymphocyte)
(cytotoxic; efficient and durable gene marking of **hematopoietic progenitor cells** in nonhuman primates after nonablative conditioning)
IT B cell (lymphocyte)

Gene therapy
Hematopoietic precursor cell
Monocyte
Polymorphonuclear leukocyte
Primate
Retroviral vectors
Signal transduction, biological
T cell (lymphocyte)
Transplant and **Transplantation**
(efficient and durable gene marking of **hematopoietic progenitor cells** in nonhuman primates after nonablative conditioning)

IT **Stem cell** factor
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(efficient and durable gene marking of **hematopoietic progenitor cells** in nonhuman primates after nonablative conditioning)

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(efficient and durable gene marking of **hematopoietic progenitor cells** in nonhuman primates after nonablative conditioning)

IT Bone marrow
Bone marrow
(**transplant**; efficient and durable gene marking of **hematopoietic progenitor cells** in nonhuman primates after nonablative conditioning)

IT 137463-76-4, PIXY321
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(efficient and durable gene marking of **hematopoietic progenitor cells** in nonhuman primates after nonablative conditioning)

IT 143011-72-7, Granulocyte colony-stimulating factor
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficient and durable gene marking of **hematopoietic progenitor cells** in nonhuman primates after nonablative conditioning)

RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L56 ANSWER 22 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **1999:582195** HCAPLUS
DN **131:256171**
TI Ex vivo expansion CD34+/AC133+ - selected autologous peripheral **blood progenitor cells** (PBPC) in high-risk breast cancer patients receiving intensive chemotherapy
AU Vavrova, J.; Filip, S.; Vokurkova, D.; Blaha, M.; Vanasek, J.; Jebavy, L.
CS Institute of Radiobiology and Immunology, Purkyne Military Medical Academy, Hradec Kralove, Czech Rep.
SO Hematology and Cell Therapy (1999), 41(3), 105-112
CODEN: HCTHFA; ISSN: 1430-2772
PB Springer-Verlag France
DT Journal
LA English
CC 15-5 (Immunochemistry)
Section cross-reference(s): 1

AB AC133 antibody provides an alternative to CD34 for the selection and characterization of cells necessary for **engraftment** in **transplant** situations. We studied the effect of **stem cell** factor (SCF), interleukin 3 (IL-3) and interleukin 11 (IL-11) on the ex vivo expansion of human CD34+/AC133+ progenitors isolated from leukapheresis products from chemotherapy plus granulocyte-colony-stimulating factor (G-CSF) -mobilized adult donors. MiniMACS AC133+ isolated cells contained a mean of 85% (80-90) AC133+ cells. Enriched AC133+ cells co-expressed CD34+ 80%, CD71low 36.6 % and **CD33**+ 6.6 %. After a seven-day ex vivo expansion in the presence of SCF + IL-3 + IL-11, the no. of cells increased 19 times. These cells expressed a mean 12% CD34+ and 74% CD71+ (23% CD 71high) and 59% **CD33**+. This means that the abs. no. of CD34+ cells increased slightly, the no. of **CD33**+ increased 100 times and cells with high d. CD71high (23%) appeared. These cells represent the cells committed to erythroid differentiation. The increase in the no. of CFU- GM with various combinations of cytokines SCF + Il-3 + IL-11 will be discussed. The no. of CFU-GM in culture after a seven-day ex vivo expansion in the presence of SCF + IL-3 + IL-11 increased 45 times.

ST chemotherapy **hematopoietic progenitor cell** AC133; **stem cell** factor leukapheresis chemotherapy; interleukin CD antigen breast chemotherapy

IT Antigens
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(AC133+; ex vivo expansion CD34+/AC133+ - selected autologous peripheral **blood progenitor cells** (PBPC) in high-risk breast cancer patients receiving intensive chemotherapy)

IT **Hematopoietic precursor cell**
(ex vivo expansion CD34+/AC133+ - selected autologous peripheral **blood progenitor cells** (PBPC) in high-risk breast cancer patients receiving intensive chemotherapy)

IT Cytokines
Stem cell factor
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(ex vivo expansion CD34+/AC133+ - selected autologous peripheral **blood progenitor cells** (PBPC) in high-risk breast cancer patients receiving intensive chemotherapy)

IT Interleukin 11
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ex vivo expansion CD34+/AC133+ - selected autologous peripheral **blood progenitor cells** (PBPC) in high-risk breast cancer patients receiving intensive chemotherapy)

IT Interleukin 3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ex vivo expansion CD34+/AC133+ - selected autologous peripheral **blood progenitor cells** (PBPC) in high-risk breast cancer patients receiving intensive chemotherapy)

IT CD antigens
CD34 (antigen)
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(ex vivo expansion CD34+/AC133+ - selected autologous peripheral **blood progenitor cells** (PBPC) in high-risk breast cancer patients receiving intensive chemotherapy)

IT **Hematopoietic precursor cell**
(granulocyte-macrophage colony-forming; ex vivo expansion CD34+/AC133+

- selected autologous peripheral **blood progenitor cells** (PBPC) in high-risk breast cancer patients receiving intensive chemotherapy)

IT Plasmapheresis
(leukapheresis; ex vivo expansion CD34+/AC133+ - selected autologous peripheral **blood progenitor cells** (PBPC) in high-risk breast cancer patients receiving intensive chemotherapy)

IT Antitumor agents
(mammary gland; ex vivo expansion CD34+/AC133+ - selected autologous peripheral **blood progenitor cells** (PBPC) in high-risk breast cancer patients receiving intensive chemotherapy)

IT Mammary gland
Mammary gland
(neoplasm, inhibitors; ex vivo expansion CD34+/AC133+ - selected autologous peripheral **blood progenitor cells** (PBPC) in high-risk breast cancer patients receiving intensive chemotherapy)

IT **Hematopoietic precursor cell**
(stem; ex vivo expansion CD34+/AC133+ - selected autologous peripheral **blood progenitor cells** (PBPC) in high-risk breast cancer patients receiving intensive chemotherapy)

IT 143011-72-7, G-CSF
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(ex vivo expansion CD34+/AC133+ - selected autologous peripheral **blood progenitor cells** (PBPC) in high-risk breast cancer patients receiving intensive chemotherapy)

IT 50-18-0, Cyclophosphamide 56420-45-2, Epirubicin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ex vivo expansion CD34+/AC133+ - selected autologous peripheral **blood progenitor cells** (PBPC) in high-risk breast cancer patients receiving intensive chemotherapy)

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L56 ANSWER 23 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **1999:534363** HCAPLUS
DN **132:117272**
TI Engineering of **hematopoietic cells** and hematopoietic

reconstitution of expanded cells in SCID mice
AU Pei, Xuetao; Liu, Ying; Feng, Kai; Li, Liang; Bai, Cixian; Wang, Xiao; Yang, Guang
CS Beijing Institute of Radiation Medicine, Beijing, 100850, Peop. Rep. China
SO Zhonghua Yixue Zazhi (1999), 79(7), 497-501
CODEN: CHHTAT; ISSN: 0376-2491
PB Zhonghua Yixue Zazhi
DT Journal
LA Chinese
CC 1-7 (Pharmacology)
AB CD34+ cells were isolated from umbilical cord blood by using a high-gradient magnetic cell sorting system (MACS), and expanded with the different combinations of cytokines in a liq. culture system to elucidate the roles of cytokines for ex vivo expansion and orderly differentiation of **hematopoietic progenitor cells**, and the capacity of hematopoietic reconstitution of the expanded cells. The expanded cells were then **transplanted** into **sublethally** irradiated SCID mice. The combination of cytokines including FL, SCF, TPO (thrombopoietin), etc. increased total cells, **progenitor cells** (CFU-GM and CFU-MK), and CD34 + CD38-early **progenitor cells** by (2 130.+-.57), (70.+-.7), and (46.+-.5) folds, resp. The percentage of dendritic cells (24.3.+-.2.1)% was also much higher than the control (0.4.+-.0.3)%. The CD34+ CD38- subsets and the combination of FL and TPO were identified as the most potential for expanding early **progenitor cells**. The expanded cells could smoothly **engraft** SCID recipients and reconstitute their hematopoiesis. Human **hematopoietic cells** could be detected in marrow cells from SCID mice **transplanted** 6 wk late. The results suggest that to expand **hematopoietic cells** ex vivo efficiently and maintain the hematopoietic reconstitution capacities of hematopoietic stem/early **progenitor cells** by an appropriate combination of cytokines is possible. The engineering of **hematopoietic cells**-the new generation of cellular therapeutics are now underway in the applications of **stem cells transplantation**, immunotherapy of cancers, and gene therapy.
ST hematopoietic system engineering cytokine immunotherapy
IT Cell differentiation
Gene therapy
Hematopoiesis
Hematopoietic precursor cell
Immunotherapy
Lymphocyte
Megakaryocyte
(engineering of **hematopoietic cells** and hematopoietic reconstitution of expanded cells in SCID mice)
IT Cytokines
Interleukin 3
Interleukin 4
Interleukin 6
Stem cell factor
Tumor necrosis factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(engineering of **hematopoietic cells** and hematopoietic reconstitution of expanded cells in SCID mice)
IT **Hematopoietic precursor cell**
(granulocyte-macrophage colony-forming; engineering of **hematopoietic cells** and hematopoietic reconstitution of expanded cells in SCID mice)
IT Immunodeficiency
(severe combined; engineering of **hematopoietic cells** and hematopoietic reconstitution of expanded cells in SCID mice)

IT 9014-42-0, Thrombopoietin 11096-26-7, Erythropoietin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(engineering of **hematopoietic cells** and hematopoietic reconstitution of expanded cells in SCID mice)

L56 ANSWER 24 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **1999:34996** HCAPLUS
DN **130:94486**
TI Recombinant effector cells expressing chimeric signalling systems and their use in disease treatment
IN Finney, Helene Margaret; Lawson, Alastair David Griffiths; Weir, Andrew Neil Charles
PA Celltech Therapeutics Limited, UK
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N015-12
ICS C07K014-705; C07K014-715; C07K014-735; C12N015-13; C07K016-28; C12N015-54; C12N009-12; C12N015-62; C07K019-00; C12N005-10; G01N033-58; G01N033-68; A61K048-00
CC 15-10 (Immunochemistry)
Section cross-reference(s): 1, 3
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9900494	A2	19990107	WO 1998-GB1842	19980624
	WO 9900494	A3	19990325		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9881210	A1	19990119	AU 1998-81210	19980624
	EP 1002073	A2	20000524	EP 1998-930934	19980624
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002511757	T2	20020416	JP 1999-505370	19980624
PRAI	GB 1997-13473	A	19970625		
	WO 1998-GB1842	W	19980624		

AB A cell activation process is described in which an effector cell is transformed with DNA coding for a chimeric receptor contg. two or more different cytoplasmic signalling components. At least one of the cytoplasmic signalling components is derived from all or part of a tetraspan-transmembrane protein, CD43, CD6, a mannose, IL-7, IL-12 or complement receptor, an integrin-assocd. protein, or a .gamma.-chain assocd. with a cytokine receptor. The activated cell may be of use in medicine for example in the treatment of diseases such as cancer. Thus, recombinant Jurkat E6.1 cells producing a chimeric receptor consisting of an anti-**CD33** single-chain Fv linked via a spacer contg. IgG1 and CD28 domains to the intracellular domain of Fc.epsilon.RI, were stimulated to produce interleukin-12 in the presence of **CD33**-pos. cells.
ST recombinant effector cell chimeric receptor disease treatment
IT Interleukin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(12, transmembrane or signalling domain of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)
IT Proteins, specific or class

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(B29, signalling domain of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)

IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD37, signalling domain of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)

IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD47, signalling domain of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)

IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD53, signalling domain of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)

IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD6, transmembrane or signalling domain of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)

IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD9, signalling domain of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CR3-assocd., signalling domain of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)

IT Immunoglobulin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IgE type I, signalling domain of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)

IT Immunoglobulin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IgG type III, signalling domain of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MB-1, signalling domain of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)

IT Antibodies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(binding domain of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)

IT Receptors
RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process)
(chimeric; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)

IT Disease, animal
(congenital, treatment of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)

IT T cell (lymphocyte)
(cytotoxic; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)

IT Disease, animal
(dermatol., treatment of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)

IT Metabolism, animal

(disorder, treatment of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)
IT Animal cell
(effector; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)
IT Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fragments, binding domain of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)
IT Glycoproteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene KAI1, signalling domain of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)
IT **Transplant** and **Transplantation**
(**graft**-vs.-host reaction, prevention of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)
IT Intestine, disease
(inflammatory, treatment of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)
IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(integrin-assocd., transmembrane or signalling domain of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)
IT Interleukin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(interleukin 12, transmembrane or signalling domain of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)
IT Interleukin receptors
Interleukin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(interleukin 15, signalling domain of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)
IT Interleukin receptors
Interleukin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(interleukin 9, signalling domain of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)
IT Lymphocyte
(natural killer cell; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)
IT Disease, animal
(neurol., treatment of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)
IT **Transplant** rejection
(prevention of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)
IT Allergy inhibitors
Anti-infective agents
Anti-inflammatory agents
Antiarthritics
Antiasthmatics
Antidiabetic agents
Antirheumatic agents
Antitumor agents
B cell (lymphocyte)
Dendritic cell
Genetic vectors
Lymphocyte

Macrophage
Monocyte
Virus vectors
(recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)

IT CD3 (antigen)
CD5 (antigen)
Cell adhesion molecules
Colony stimulating factor receptors
Immunoglobulin receptors
Interleukin 4 receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(signalling domain of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)

IT **Hematopoietic precursor cell**
(stem; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)

IT CD28 (antigen)
CD4 (antigen)
CD8 (antigen)
TCR (T cell receptors)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(transmembrane domain of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)

IT Complement receptors
Cytokine receptors
Interleukin 7 receptors
Leukosialin
Mannose receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(transmembrane or signalling domain of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)

IT Cystic fibrosis
Eczema
Multiple sclerosis
Psoriasis
Sickle cell anemia
(treatment of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)

IT Complement receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type 1, signalling domain of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)

IT Interleukin 2 receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha.-chain, signalling domain of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)

IT 80449-02-1, Tyrosine kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(signalling domain of; recombinant effector cells expressing chimeric signalling systems and their use in disease treatment)

L56 ANSWER 25 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **1998:816003** HCAPLUS
DN **130:51353**
TI Method for production of monoclonal antibodies in chimeric mice or rats having xenogeneic antibody-producing cells
IN **Reisner, Yair**
PA Yeda Research and Development Co. Ltd., Israel
SO U.S., 34 pp., Cont.-in-part of U.S. Ser. No. 347,116, abandoned.
CODEN: USXXAM

DT Patent
LA English
IC ICM A01N053-00
ICS A61K049-00; C12N005-00; C12N005-16
NCL 424093210
CC 15-3 (Immunochemistry)
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5849288	A	19981215	US 1995-475584	19950607
	IL 93067	A1	19951231	IL 1990-93067	19900115
	JP 04267830	A2	19920924	JP 1991-309255	19911125
	JP 2647292	B2	19970827		
	US 5652373	A	19970729	US 1993-61706	19930517
PRAI	IL 1990-93067	A	19900115		
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	US 1993-61706	A3	19930517		
	US 1994-347116	B2	19941123		

AB Non-human chimeric mammals are created from a mammal having **hematopoietic cells** replaced with **hematopoietic cells** from a hematopoietic deficient mammal donor, and in which xenogeneic **hematopoietic cells** and/or tissue are **engrafted**. The chimeric mammal can produce xenogeneic, preferably human, B and/or T cells, and can be used as a source of mammalian, preferably human, monoclonal antibodies and/or T cells.

ST monoclonal antibody chimeric mouse **hematopoietic cell**

IT Lymphoma
(B-cell, cell; prodn. of monoclonal antibodies in chimeric mice or rats having xenogeneic antibody-producing cells)

IT Immunodeficiency
(T or B cell; prodn. of monoclonal antibodies in chimeric mice or rats having xenogeneic antibody-producing cells)

IT Immunity
(autoimmunity, cells; prodn. of monoclonal antibodies in chimeric mice or rats having xenogeneic antibody-producing cells)

IT Leukemia
(cell; prodn. of monoclonal antibodies in chimeric mice or rats having xenogeneic antibody-producing cells)

IT Intestine
(colon, cells; prodn. of monoclonal antibodies in chimeric mice or rats having xenogeneic antibody-producing cells)

IT T cell (lymphocyte)
(cytotoxic; prodn. of monoclonal antibodies in chimeric mice or rats having xenogeneic antibody-producing cells)

IT **Transplant and Transplantation**
(**graft**-vs.-host reaction; prodn. of monoclonal antibodies in chimeric mice or rats having xenogeneic antibody-producing cells)

IT Hepatitis B virus
Hepatitis C virus
(human; prodn. of monoclonal antibodies in chimeric mice or rats having xenogeneic antibody-producing cells)

IT B cell (lymphocyte)
T cell (lymphocyte)
(immunodeficiency; prodn. of monoclonal antibodies in chimeric mice or rats having xenogeneic antibody-producing cells)

IT **Transplant and Transplantation**
(liver; prodn. of monoclonal antibodies in chimeric mice or rats having xenogeneic antibody-producing cells)

IT Lymphocyte
(lymphokine-activated killer cell; prodn. of monoclonal antibodies in

chimeric mice or rats having xenogeneic antibody-producing cells)
IT Blood cell
(malignant; prodn. of monoclonal antibodies in chimeric mice or rats having xenogeneic antibody-producing cells)
IT Antibodies
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monoclonal; prodn. of monoclonal antibodies in chimeric mice or rats having xenogeneic antibody-producing cells)
IT Domestic animal
Human immunodeficiency virus
Mammal (Mammalia)
Mitogens
Mouse
Neoplasm
Pathogen
Rat
Virus
(prodn. of monoclonal antibodies in chimeric mice or rats having xenogeneic antibody-producing cells)
IT Immunoglobulins
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(prodn. of monoclonal antibodies in chimeric mice or rats having xenogeneic antibody-producing cells)
IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prodn. of monoclonal antibodies in chimeric mice or rats having xenogeneic antibody-producing cells)
IT Toxins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prodn. of monoclonal antibodies in chimeric mice or rats having xenogeneic antibody-producing cells)
IT Immunodeficiency
(severe combined; prodn. of monoclonal antibodies in chimeric mice or rats having xenogeneic antibody-producing cells)
IT Toxoids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(tetanus; prodn. of monoclonal antibodies in chimeric mice or rats having xenogeneic antibody-producing cells)
IT Liver
Lymph node
Spleen
Thymus gland
(**transplant**; prodn. of monoclonal antibodies in chimeric mice or rats having xenogeneic antibody-producing cells)
IT **Hematopoietic precursor cell**
(xenogeneic; prodn. of monoclonal antibodies in chimeric mice or rats having xenogeneic antibody-producing cells)
IT **Transplant and Transplantation**
(**xenotransplant**; prodn. of monoclonal antibodies in chimeric mice or rats having xenogeneic antibody-producing cells)
IT 51-28-5, Dinitrophenol, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prodn. of monoclonal antibodies in chimeric mice or rats having xenogeneic antibody-producing cells)
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L56 ANSWER 26 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **1998:643039** HCAPLUS
DN **130:1956**
TI Serum-free ex vivo expansion of CD34+ **hematopoietic progenitor cells**
AU Mobest, Dieter; Mertelsmann, Roland; Henschler, Reinhard
CS Experimental Hematology Group, Department of Hematology/Oncology, University Medical Center, Freiburg, Germany
SO Biotechnology and Bioengineering (1998), 60(3), 341-347
CODEN: BIBIAU; ISSN: 0006-3592
PB John Wiley & Sons, Inc.
DT Journal
LA English
CC 9-11 (Biochemical Methods)
Section cross-reference(s): 14
AB In an effort to obtain defined culture conditions for ex vivo expansion of hematopoietic stem and **progenitor cells** which avoid the supplementation of serum, we cultured human CD34+ **hematopoietic progenitor cells** in a chem. defined, serum-free medium in the presence of hematopoietic growth factors (HGFs), **stem cell** factor (SCF), interleukin (IL)-1.beta., IL-3, IL-6, and erythropoietin (EPO). A medium, SFM-1, was prepd. according to a protocol previously optimized for semisolid **progenitor cell** assays contg. Iscove's Modified Dulbecco's Medium (IMDM) plus cholesterol, bovine serum albumin, transferrin, nucleotides and nucleosides, insulin, and .beta.-mercaptoethanol. In static cultures seeded with CD34+-enriched **progenitor cells** isolated from human peripheral blood, a mean 76.6-fold expansion of total nucleated cells and a mean 4.6-fold expansion of colony-forming cells (CFC) was recorded after 14 days. Morphol. anal. of the expanded cells revealed formation of myeloid, erythroid, and megakaryocytic cells. Flow cytometric anal. indicated that CD34+ antigen expressing cells were maintained to a limited degree only, and cell populations expressing surface markers for myeloid (**CD33**, CD14, and CD15) and megakaryocytic (CD41a) lineages predominated.

Within SFM-1, bovine serum albumin (BSA), cholesterol, and transferrin represented the most crit. components needed for efficient total cell and CFC expansion. Addn. of autologous patient plasma (APP) or fetal calf serum (FCS) to SFM-1 resulted in inferior cell amplification and CFC formation compared to controls in SFM-1, indicating that the components used in SFM-1 could replace exogenous serum. Four com. available serum-free media resulted in either comparable or lower total cell and CFC yields as SFM-1. The **transplantation** potential of CD34+ cells after culture in SFM-1 was assayed using limiting diln. anal. on preformed irradiated bone marrow stroma and revealed maintenance of long-term bone marrow culture initiating cell (LTCIC) levels during the culture period. These data indicate that HGF-supported multilineage ex vivo expansion of human CD34+ **hematopoietic progenitor cells** is feasible using an IMDM-based culture medium which contains a restricted no. of additives, resulting in analogous or improved yields of both primitive and differentiated cells compared to previously established protocols. We suggest that this culture protocol is of advantage when working with pharmaceutical-grade prepns. under serum-free conditions.

ST **hematopoietic progenitor cell** serum free medium bone marrow **transplantation**

IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**CD33** and CD41a; serum-free ex vivo expansion of CD34+ **hematopoietic progenitor cells**)

IT Blood-group substances
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Lex; serum-free ex vivo expansion of CD34+ **hematopoietic progenitor cells**)

IT **Transplant** and **Transplantation**
(bone marrow; serum-free ex vivo expansion of CD34+ **hematopoietic progenitor cells**)

IT Animal tissue culture
(mammalian; serum-free ex vivo expansion of CD34+ **hematopoietic progenitor cells**)

IT Culture media
Hematopoietic precursor cell
(serum-free ex vivo expansion of CD34+ **hematopoietic progenitor cells**)

IT Hemopoietins
Interleukin 1.beta.
Interleukin 3
Interleukin 6
Nucleosides, biological studies
Nucleotides, biological studies
Stem cell factor
Transferrins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(serum-free ex vivo expansion of CD34+ **hematopoietic progenitor cells**)

IT CD14 (antigen)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(serum-free ex vivo expansion of CD34+ **hematopoietic progenitor cells**)

IT Albumins, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(serum; serum-free ex vivo expansion of CD34+ **hematopoietic progenitor cells**)

IT Embryo, animal
(**stem cell**; serum-free ex vivo expansion of CD34+ **hematopoietic progenitor cells**)

IT Bone marrow

(**transplant**; serum-free ex vivo expansion of CD34+ **hematopoietic progenitor cells**)

IT 57-88-5, Cholesterol, biological studies 60-24-2, .beta.-Mercaptoethanol 9004-10-8, Insulin, biological studies 11096-26-7, Erythropoietin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(serum-free ex vivo expansion of CD34+ **hematopoietic progenitor cells**)

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L56 ANSWER 27 OF 48 HCAPLUS COPYRIGHT 2002 ACS

AN **1998:599327** HCAPLUS

DN **130:3023**

TI CD34+ cell dose and **CD33**- subsets: collection and **engraftment** kinetics in autologous peripheral blood **stem cells transplantation**

AU Mayol, Antonia Sampol; Vital, Joan Besalduch; Llodra, Antoni Galmes; Lleonart, Joan Bargay; Flori, Nuria Matamoros; Sureda, Miquel Morey; Garcia, Andres Novo; Riera, Marti Mascaro; Bach, Elena Gonzalez; Garcia, Pedro Martinez

CS Servicio de Hematologia y Hemoterapia y, Palma de Mallorca, Spain

SO Haematologica (1998), 83(6), 489-495
CODEN: HAEMAX; ISSN: 0390-6078

PB Il Pensiero Scientifico Editore

DT Journal

LA English

CC 15-10 (Immunochemistry)

AB We analyzed the factors that affected the no. and quality of peripheral blood **stem cells** (PBSC) collected for **transplant** in order to establish a min. threshold for rapid hematopoietic recovery. From Jan. 1995 to Nov. 1996, a consecutive series of 67 patients, with hematol. and solid tumors underwent autologous PBSC **transplantation**. Collection of PBSC was performed after mobilization with granulocyte-colony stimulating factor (G-CSF) or with chemotherapy (CT) plus G-CSF. We calcd. the factors that influenced PBSC collection, the kinetics of granulocyte and platelet recovery and the threshold value of CD34+ cells for a rapid recovery. The data were analyzed by means of multivariate Cox regression model and the receiver operating characteristic (ROC) methodol. Our results showed that mobilization with chemotherapy plus G-CSF was assocd. with a higher yield

of PBSC in comparison with mobilization with G-CSF alone. Disease status, fewer cycles of conventional prior chemotherapy and absence of prior radiation therapy also influenced the yield of PBSC. The no. of CD34+ cells, CD34+**CD33**- cell subsets, the mobilization schedule, and the conditioning regimen correlated significantly with time to hematopoietic recovery. In the multivariate anal. only the CD34+ **CD33**- cell content and the total no. of CD34+ were related with rapid neutrophil and platelet recovery, resp. Use of G-CSF after **transplant** significantly shortened the neutrophil recovery time only in patients **transplanted** with suboptimal dose of PBSC. These data suggest the utility of quantitation of CD34+ cells subsets to predict quick **engraftment**.

ST **stem cell transplantation** CD34 hematopoiesis neutrophil platelet

IT Chemotherapy
Hematopoiesis
Neutrophil
Platelet (blood)
Transplant and **Transplantation**
(CD34+ cell dose and **CD33**- subsets in relation to collection and **engraftment** kinetics in autologous peripheral blood **stem cells transplantation**)

IT CD34 (antigen)
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(CD34+ cell dose and **CD33**- subsets in relation to collection and **engraftment** kinetics in autologous peripheral blood **stem cells transplantation**)

IT **Hematopoietic precursor cell**
(stem; CD34+ cell dose and **CD33**- subsets in relation to collection and **engraftment** kinetics in autologous peripheral blood **stem cells transplantation**)

IT 143011-72-7, Colony-stimulating factor, granulocyte
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(CD34+ cell dose and **CD33**- subsets in relation to collection and **engraftment** kinetics in autologous peripheral blood **stem cells transplantation**)

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L56 ANSWER 28 OF 48 HCAPLUS

AN 1997:684303 HCAPLUS
DN 127:358050
TI Novel product and process for T lymphocyte **veto**
IN Staerz, Uwe D.
PA National Jewish Center for Immunology and Respiratory Medicine, USA; Staerz, Uwe D.
SO PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K039-395
ICS C12N005-10; C12N015-12; C12N015-13; C12P021-08
CC 15-2 (Immunochemistry)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9737687	A1	19971016	WO 1997-US5943	19970410
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 6060054	A	20000509	US 1996-630172	19960410
	CA 2251819	AA	19971016	CA 1997-2251819	19970410
	AU 9727258	A1	19971029	AU 1997-27258	19970410
	EP 929316	A1	19990721	EP 1997-921134	19970410
	R: CH, DE, FR, GB, IT, LI, SE				
	US 6264950	B1	20010724	US 1999-375419	19990817
PRAI	US 1996-630172	A2	19960410		
	WO 1997-US5943	W	19970410		

AB The present invention relates to a product and process for suppressing an immune response using a T lymphocyte **veto** mol. capable of blocking cell surface mols. responsible for T cell activation. Disclosed is a CD4 or CD2 mol., assocd. with an Ig mol. capable of binding to a major histocompatibility antigen. The CD2 or CD4 mol. may also be replaced by CTLA4, Fas ligand, CD5, CD7, CD9, CD11, CD18, CD27, CD43, CD45. CD48, B7.1 or B7.2 protein. Also disclosed is a method to produce a T lymphocyte **veto** mol., a therapeutic compn. comprising a T lymphocyte **veto** mol. and methods to use T lymphocyte **veto** mols. in therapeutic processes requiring suppression of an immune response.

ST immunosuppressant chimeric protein T lymphocyte **veto**; CD2 CD4 fusion protein immunosuppression **transplant**

IT CD antigens
CD antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CD11, fusion protein; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT CD antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CD27, fusion protein; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(CD48 fusion protein; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT CD antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CD9, fusion protein; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(G2a, fusion protein; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LMA, fusion protein contg.; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(MHC (major histocompatibility complex), class I; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(MHC (major histocompatibility complex); chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Epitopes
(MHC complex; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(RCA fusion protein; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Glycoproteins, specific or class
Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SU (surface), fusion protein contg.; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Integrins
Integrins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antigens CD11, fusion protein; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Thyroid gland, disease
(autoimmune thyroiditis; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Immunity
(autoimmunity; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bile acid, fusion protein contg.; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Proteins, general, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(blood; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)
IT Addison's disease
Affinity chromatography
Autoimmune disease
CD4-positive T cell
Celiac disease
Electrophoresis
Gel permeation chromatography
Graves' disease
Multiple sclerosis
Myasthenia gravis
Pancreatic islet of Langerhans
Protein sequences
Reversed phase chromatography
Rheumatoid arthritis
Transplant and **Transplantation**
Transplant rejection
(chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)
IT Fusion proteins (chimeric proteins)
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)
IT Liquid chromatography
(focusing; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)
IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fusion protein contg. tissue-specific; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)
IT Asialoglycoprotein receptors
c-Kit (protein)
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fusion protein contg.; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)
IT Growth factors, animal
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fusion protein contg.; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)
IT Baboon
Cat (Felis catus)
Cattle
Dog (Canis familiaris)
Goat
Hamster
Horse (Equus caballus)
Mouse
Rabbit
Rat
Swine
(fusion protein; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)
IT CD2 (antigen)
CD28 (antigen)
CD4 (antigen)
CD45 (antigen)

CD5 (antigen)
CD7 (antigen)
CD80 (antigen)
CD86 (antigen)
CTLA-4 (antigen)
Fas ligand
Immunoglobulins
Leukosialin
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fusion protein; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Drug delivery systems
(inhalants; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Drug delivery systems
(injections, i.v.; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Diabetes mellitus
(insulin-dependent; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Drug delivery systems
(intraarticular; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Drug delivery systems
(intracranial; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Heart
(myocyte, fusion protein; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Drug delivery systems
(nasal; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Nerve
(neuron, recombinant cell; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Primate
(non-human fusion protein; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Drug delivery systems
(oral; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Bile acids
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(receptor, fusion protein contg.; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Animal cell line
(recombinant T; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT B cell (lymphocyte)
(recombinant cell line; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Epithelium
(recombinant cell; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Fibroblast
(recombinant; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Drug delivery systems
(rectal; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

IT Heart, disease
(rheumatoid carditis; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)
IT Drug delivery systems
Drug delivery systems
(solns., i.p.; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)
IT **Hematopoietic precursor cell**
(stem, recombinant; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)
IT Lupus erythematosus
(systemic; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)
IT Drug delivery systems
(topical; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)
IT Drug delivery systems
(transdermal; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)
IT T cell (lymphocyte)
(**veto** mol.; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)
IT Integrins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(.beta.2, fusion protein; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)
IT 1306-06-5, Hydroxyapatite
RL: BUU (Biological use, unclassified); DEV (Device component use); BIOL (Biological study); USES (Uses)
(adsorption; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)
IT 132729-32-9, Antigen B 7 (mouse clone pB7 precursor protein moiety reduced) 198651-08-0 198651-09-1 198651-10-4 198652-30-1 198652-31-2 198652-32-3 198652-33-4 198652-34-5 198652-35-6, CD5 (antigen) (human fragment) 198652-36-7 198652-37-8 198652-38-9 198652-39-0 198652-40-3 198652-41-4 198652-42-5 198652-43-6 198652-44-7 198652-45-8 198652-46-9
RL: PRP (Properties)
(amino acid sequence; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)
IT 68181-17-9
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(as linker; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)
IT 9002-60-2, Corticotropin, biological studies 9002-71-5, Thyroid stimulating hormone 11000-17-2, Vasopressin
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chimeric immunosuppressing protein contg.; chimeric proteins contg. CD2 or CD4 and Ig. for T lymphocyte **veto** or immunosuppression)

L56 ANSWER 29 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:664936 HCAPLUS
DN 127:341440
TI Multilineage long-term **engraftment** potential of drug-resistant hematopoietic progenitors
AU Bertolini, Francesco; Battaglia, Manuela; Lanza, Annalisa; Gibelli, Nadia; Palermo, Belinda; Pavesi, Lorenzo; Caprotti, Marco; Robustelli della Cuna, Gioacchino

CS Division of Medical Oncology, IRCCS Maugeri Foundation, Pavia Medical Center, Pavia, 27100, Italy
SO Blood (1997), 90(8), 3027-3036
CODEN: BLOOAW; ISSN: 0006-4971
PB Saunders
DT Journal
LA English
CC 1-6 (Pharmacology)
AB Peripheral **blood progenitor cells** (PBPCs) are increasingly used instead of bone marrow for autologous or **allogeneic transplantation**. In this study PBPCs mobilized in cancer patients by chemotherapy and granulocyte-colony stimulating factor were collected by apheresis and first enriched by immunoaffinity removal of lineage pos. cells. When these cells were exposed to both cyclophosphamide and taxol or cultured for 7 days in the presence of 5-fluorouracil, **stem cell** factor, and interleukin-3, 88% to 93% of the enriched PBPCs were killed and short-term clonogenic capacity in methylcellulose assays was lost, but week-5 cobblestone area-forming cell (CAFC) enrichment was higher than 10-fold in comparison to enriched PBPCs and higher than 700-fold in comparison to unmanipulated apheresis cells. After drug exposure, most of the progenitors displayed a CD34+, CD38-, multidrug-resistance (MDR+), Rhodamine 123 low, Hoechst 33342 low phenotype, and as few as 180 of these drug-resistant cells were able to generate a stable multilineage human hematopoiesis in **sublethally** irradiated immunodeficient mice. In these animals, the level of human hematopoietic **engraftment** was significantly increased by **cotransplantation** of irradiated cells from the human L87/4 stromal cell line. These observations are consistent with the functional isolation of a population of very early hematopoietic progenitors and might help to design new protocols for the removal of neoplastic cells from **autografts**.
ST antitumor resistance hematopoietic progenitor bone **transplant**
IT Drug resistance
(antitumor; multilineage long-term **engraftment** potential of drug-resistant hematopoietic progenitors)
IT **Transplant and Transplantation**
(bone marrow; multilineage long-term **engraftment** potential of drug-resistant hematopoietic progenitors)
IT Antitumor agents
(leukemia; multilineage long-term **engraftment** potential of drug-resistant hematopoietic progenitors)
IT **Hematopoietic precursor cell**
(multilineage long-term **engraftment** potential of drug-resistant hematopoietic progenitors)
IT Interleukin 3
Stem cell factor
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(multilineage long-term **engraftment** potential of drug-resistant hematopoietic progenitors)
IT Antitumor agents
(resistance to; multilineage long-term **engraftment** potential of drug-resistant hematopoietic progenitors)
IT Bone marrow
(**transplant**; multilineage long-term **engraftment** potential of drug-resistant hematopoietic progenitors)

L56 ANSWER 30 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **1997:606623** HCAPLUS
DN **127:189652**
TI **Engraftment** and development of xenogeneic cells in normal mammals having reconstituted hematopoiesis-deficient immune systems
IN **Reisner, Yair**

PA Yeda Research and Development Co., Ltd., Israel
SO U.S., 31 pp., Cont.-in-part of U. S. Ser. No. 892,911, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC A61K049-00; A61K035-12; C12N015-01
NCL 800002000
CC 15-1 (Immunochemistry)
Section cross-reference(s): 8
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5652373	A	19970729	US 1993-61706	19930517
	IL 93067	A1	19951231	IL 1990-93067	19900115
	JP 04267830	A2	19920924	JP 1991-309255	19911125
	JP 2647292	B2	19970827		
	CA 2161798	AA	19941208	CA 1994-2161798	19940513
	WO 9427556	A2	19941208	WO 1994-US5410	19940513
	WO 9427556	A3	19950608		
	W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KG, KR, KZ, LK, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, UA, UZ, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9469499	A1	19941220	AU 1994-69499	19940513
	EP 699235	A1	19960306	EP 1994-917988	19940513
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	US 5849987	A	19981215	US 1994-242580	19940513
	JP 3064421	B2	20000712	JP 1995-500728	19940513
	JP 08511937	T2	19961217		
	US 5858328	A	19990112	US 1994-337925	19941110
	US 5849288	A	19981215	US 1995-475584	19950607
	US 5866757	A	19990202	US 1996-744769	19961106
	US 5804160	A	19980908	US 1997-832172	19970408
PRAI	IL 1990-93067	A	19900115		
	US 1990-618303	B2	19901126		
	IL 1991-98369	A	19910604		
	US 1991-792480	B2	19911115		
	US 1992-892911	B2	19920603		
	US 1993-61706	A	19930517		
	IL 1993-106951	A	19930908		
	WO 1994-US5410	W	19930908		
	US 1994-242580	A2	19940513		
	US 1994-337925	A	19941110		
	US 1994-347088	A2	19941123		
	US 1994-347116	B2	19941123		

AB Non-human chimeric mammals are created from a mammal having **hematopoietic cells** replaced with **hematopoietic cells** from a hematopoiesis-deficient mammal donor, and optionally in which xenogeneic cells and/or tissue are **engrafted**. The xenogeneic, preferably human, cells or tissue may be **hematopoietic cells**, in which case the chimeric mammal can produce xenogeneic B and/or T cells, and can be used as a source of mammalian, preferably human, monoclonal antibodies and/or T cells. Alternatively, the xenogeneic cells or tissue may be non-hematopoietic, such as normal or pathol. cells or tissue, which can form a stable **transplant** in the chimeric mammal and thus can be used as an animal model of various pathologies or to test therapeutic or diagnostic agents or modalities. Such animals can be used as a source of human monoclonal antibodies and cytotoxic T cells.
ST chimeric animal hematopoiesis immunodeficiency **xenotransplant** antibody
IT Radiation
(-induced immunodeficiency; **engraftment** and development of

xenogeneic cells in normal mammals having reconstituted hematopoiesis-deficient immune systems)
IT Immunodeficiency
(B-cell; **engraftment** and development of xenogeneic cells in normal mammals having reconstituted hematopoiesis-deficient immune systems)
IT Immunodeficiency
(T-cell; **engraftment** and development of xenogeneic cells in normal mammals having reconstituted hematopoiesis-deficient immune systems)
IT Liver
Lymph node
(cells of; **engraftment** and development of xenogeneic cells in normal mammals having reconstituted hematopoiesis-deficient immune systems)
IT Mouse
Rat
(chimeric; **engraftment** and development of xenogeneic cells in normal mammals having reconstituted hematopoiesis-deficient immune systems)
IT T cell (lymphocyte)
(cytotoxic, prodn. of; **engraftment** and development of xenogeneic cells in normal mammals having reconstituted hematopoiesis-deficient immune systems)
IT Blood cell
Bone marrow
Hematopoiesis
Hematopoietic precursor cell
Leukemia
Leukocyte
Neoplasm
(**engraftment** and development of xenogeneic cells in normal mammals having reconstituted hematopoiesis-deficient immune systems)
IT B cell (lymphocyte)
T cell (lymphocyte)
(immunodeficiency involving; **engraftment** and development of xenogeneic cells in normal mammals having reconstituted hematopoiesis-deficient immune systems)
IT Hepatitis
(liver cells from human with; **engraftment** and development of xenogeneic cells in normal mammals having reconstituted hematopoiesis-deficient immune systems)
IT Antibodies
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monoclonal, prodn. of; **engraftment** and development of xenogeneic cells in normal mammals having reconstituted hematopoiesis-deficient immune systems)
IT Immunodeficiency
(severe combined, murine; **engraftment** and development of xenogeneic cells in normal mammals having reconstituted hematopoiesis-deficient immune systems)
IT Spleen
(splenocyte; **engraftment** and development of xenogeneic cells in normal mammals having reconstituted hematopoiesis-deficient immune systems)
IT Thymus gland
(thymocyte; **engraftment** and development of xenogeneic cells in normal mammals having reconstituted hematopoiesis-deficient immune systems)
IT **Transplant and Transplantation**
(**xenotransplant**; **engraftment** and development of xenogeneic cells in normal mammals having reconstituted

hematopoiesis-deficient immune systems)

L56 ANSWER 31 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:254226 HCAPLUS
DN 126:316070
TI A synthetic CD4-CDR3 peptide analog **enhances** bone marrow **engraftment** across major histocompatibility barriers
AU Koch, Ute; Korngold, Robert
CS Kimmel Cancer Inst., Jefferson Med. Coll., Philadelphia, PA, 19107, USA
SO Blood (1997), 89(8), 2880-2890
CODEN: BLOOAW; ISSN: 0006-4971
PB Saunders
DT Journal
LA English
CC 15-2 (Immunochemistry)
AB The efficacy of a synthetic peptide analog mimicking the CDR3-D1 domain of the CD4 mol. was investigated in murine models of **allogeneic** bone marrow **engraftment** after **transplantation** across major histocompatibility complex (MHC) barriers. A single dose of a CD4-CDR3 peptide analog was administered at the time of marrow **transplantation** to three different **allogeneic** mouse strain combinations after appropriate **sublethal** total body irradn.: (1) B10.BR .fwdarw. C57BL/6J (B6), a full **allogeneic** MHC difference; (2) (B6xDBA/2)F1 .fwdarw. (B6xCBA)F1, a haploidentical MHC combination; and (3) B6.C-H2bm12 .fwdarw. B6-Ly5.2, involving only a MHC class II difference. Donor-host chimerism was assessed after 1 and 2 mo **posttransplantation** by flow cytometric anal. of spleen and/or lymph node cells. Peptide-treated animals in all three strain combinations exhibited significantly **enhanced** donor lymphoid **engraftment**, which was similarly reflected in the total lymphocyte compartment and its T-cell (CD4+, CD8+) and B-cell subsets. In addn., peptide-treated mice in the haploidentical and MHC class II-mismatched strain combinations exhibited prolonged **tolerance** of both donor and syngeneic host-type tail skin **grafts** while rejecting third-party **allogeneic grafts**, thus supporting the reconstitution of immunocompetence in these chimeras. Lymphocytes from the peptide-treated haploidentical chimeric mice also displayed donor-specific **tolerance** upon stimulation in a one-way mixed lymphocyte reaction. In a 6-day colony-forming unit-granulocyte-macrophage (CFU-GM) assay to quantitate the level of **hematopoietic cell engraftment** in both the haploidentical and class II-disparate strain combinations, bone marrow cells from the peptide-treated mice exhibited significant increases in CFU-GM compared with the saline-treated control groups. Finally, early multiple treatments with the peptide after **transplantation** significantly **enhanced** donor chimerism in donor-presensitized recipient mice across the MHC class II barrier and proved to be significantly more effective than anti-CD4 monoclonal antibody treatment. These results indicate that the structure-based CD4-CDR3 peptide analog may represent a valuable approach to the inhibition of **graft rejection** after MHC-mismatched bone marrow **transplantation**.
ST CD4 CDR3 peptide analog marrow **engraftment**
IT Histocompatibility antigens
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(MHC (major histocompatibility complex), class II; synthetic CD4-CDR3 peptide analog **enhances** bone marrow **engraftment** across major histocompatibility barriers)
IT **Transplant and Transplantation**
(bone marrow; synthetic CD4-CDR3 peptide analog **enhances** bone marrow **engraftment** across major histocompatibility barriers)
IT **Immune tolerance**
(synthetic CD4-CDR3 peptide analog **enhances** bone marrow

engraftment across major histocompatibility barriers)
IT Bone marrow
(**transplant**; synthetic CD4-CDR3 peptide analog **enhances** bone marrow **engraftment** across major histocompatibility barriers)
IT 157566-11-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthetic CD4-CDR3 peptide analog **enhances** bone marrow **engraftment** across major histocompatibility barriers)

L56 ANSWER 32 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **1996:494563** HCAPLUS
DN **125:140566**
TI **Engraftment** of **hematopoietic cells** from a primate donor to a primate recipient
IN **Reisner, Yair**
PA Yeda Research and Development Co. Ltd., Israel
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 15-10 (Immunochemistry)
Section cross-reference(s): 3
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9619965	A2	19960704	WO 1995-US16850	19951222
	W: CA, JP, KR, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2208719	AA	19960704	CA 1995-2208719	19951222
	EP 820309	A2	19980128	EP 1995-944392	19951222
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	JP 10511552	T2	19981110	JP 1995-520571	19951222
PRAI	IL 1994-112109		19941222		
	WO 1995-US16850		19951222		

AB A method for the replacement of the hematopoietic system of one primate with a hematopoietic system derived from another primate of a different species. The method comprises **xenograft** of T cell-depleted bone marrow prepn. or peripheral **stem cell** prepn. from monkey to human or human to monkey. The method is useful for treating cancer patient undergoing chemotherapy, for producing antibodies or cytotoxic T cells, for studying efficacy of a therapeutic agent against sickle cell anemia, thalassemia, HIV infection, leukemia, lymphoma, and malaria, and for genetherapy.
ST **xenotransplant hematopoietic cell** primate human monkey
IT Bone marrow
(T cell-depleted prepn. of; **engraftment** of **hematopoietic cells** from a primate donor to a primate recipient)
IT Blood corpuscle
Eukaryote
Hematopoietic precursor cell
Leukemia
Lymphoma
Malaria
Monkey
Neoplasm
Primate
Prokaryote

Sickle cell anemia
Thalassemia
(**engraftment** of **hematopoietic cells** from a primate donor to a primate recipient)

IT Antibodies
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**engraftment** of **hematopoietic cells** from a primate donor to a primate recipient)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**engraftment** of **hematopoietic cells** from a primate donor to a primate recipient)

IT Virus
(infection; **engraftment** of **hematopoietic cells** from a primate donor to a primate recipient)

IT Animal cell
Animal tissue
(pathogenic; **engraftment** of **hematopoietic cells** from a primate donor to a primate recipient)

IT Lymphocyte
(B-cell, **engraftment** of **hematopoietic cells** from a primate donor to a primate recipient)

IT Lymphocyte
(T-cell, **engraftment** of **hematopoietic cells** from a primate donor to a primate recipient)

IT Lymphocyte
(T-cell, cytotoxic, **engraftment** of **hematopoietic cells** from a primate donor to a primate recipient)

IT Therapeutics
(chemo-, **engraftment** of **hematopoietic cells** from a primate donor to a primate recipient)

IT Therapeutics
(geno-, **engraftment** of **hematopoietic cells** from a primate donor to a primate recipient)

IT Leukocyte
(granulocyte, **engraftment** of **hematopoietic cells** from a primate donor to a primate recipient)

IT Virus, animal
(human immunodeficiency, **engraftment** of **hematopoietic cells** from a primate donor to a primate recipient)

IT Antibodies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal, **engraftment** of **hematopoietic cells** from a primate donor to a primate recipient)

IT Microorganism
(pathogenic, **engraftment** of **hematopoietic cells** from a primate donor to a primate recipient)

IT Virus, animal
(retro-, **engraftment** of **hematopoietic cells** from a primate donor to a primate recipient)

IT **Hematopoietic precursor cell**
(stem, peripheral; **engraftment** of **hematopoietic cells** from a primate donor to a primate recipient)

IT **Transplant and Transplantation**
(xeno-, **engraftment** of **hematopoietic cells** from a primate donor to a primate recipient)

IT 143011-72-7, G-CSF
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**engraftment** of **hematopoietic cells** from a primate donor to a primate recipient)

L56 ANSWER 33 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **1996:332981** HCAPLUS
DN **125:4607**
TI **Nonlethal** methods for conditioning a recipient for bone marrow **transplantation** using **sublethal** doses of total body irradiation, cell type-specific antibodies, cytotoxic drugs, or a combination thereof
IN Ildstad, Suzanne T.
PA University of Pittsburgh, USA
SO U.S., 21 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K043-00
ICS A61K031-00; A61N005-00
NCL 424001490
CC 8-9 (Radiation Biochemistry)
Section cross-reference(s): 1, 15
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5514364	A	19960507	US 1993-120256	19930913
	US 5635156	A	19970603	US 1994-337785	19941114
	US 5876692	A	19990302	US 1997-785070	19970117
	US 6217867	B1	20010417	US 1998-177704	19981022
	US 2001009663	A1	20010726	US 1999-245038	19990205
PRAI	US 1993-120256	A2	19930913		
	US 1994-337785	A3	19941114		
	US 1997-785070	A2	19970117		
	US 1998-73764P	P	19980205		
	US 1998-177704	A2	19981023		

AB **Nonlethal** methods of conditioning a recipient for bone marrow **transplantation** are provided. In particular, the invention relates to the use of **sublethal** doses of total body irradn., cell type-specific antibodies, esp. antibodies directed to bone marrow stromal cell markers, cytotoxic drugs, or a combination thereof. The methods of the invention have a wide range of applications, including, but not limited to, the conditioning of an individual for hematopoietic reconstitution by bone marrow **transplantation** for the treatment of hematol. malignancies, hematol. disorders, autoimmunity, infectious diseases (e.g. acquired immunodeficiency syndrome), and the **engraftment** of bone marrow cells to induce **tolerance** for solid organ, tissue and cellular **transplantation**.
ST bone marrow **transplant** recipient conditioning; cytotoxic agent bone marrow **transplant** conditioning; radiation antibody bone marrow **transplant** conditioning
IT Lymphocyte
(anti-lymphocyte globulin; **nonlethal** methods for conditioning recipient for bone marrow **transplant** using **sublethal** doses of total body irradn., cell type-specific antibodies, cytotoxic drugs, or combination)
IT Macrophage
(antibody to; **nonlethal** methods for conditioning recipient for bone marrow **transplant** using **sublethal** doses of total body irradn., cell type-specific antibodies, cytotoxic drugs, or combination)
IT Cell proliferation
(antibody-antiproliferative agent conjugates; **nonlethal** methods for conditioning recipient for bone marrow **transplant** using **sublethal** doses of total body irradn., cell type-specific antibodies, cytotoxic drugs, or combination)
IT **Hematopoietic precursor cell**

(facilitatory, antibody to; **nonlethal** methods for conditioning recipient for bone marrow **transplant** using **sublethal** doses of total body irradn., cell type-specific antibodies, cytotoxic drugs, or combination)

IT Alkylating agents, biological
Blood platelet
Erythrocyte
Immune **tolerance**
Radiation
(**nonlethal** methods for conditioning recipient for bone marrow **transplant** using **sublethal** doses of total body irradn., cell type-specific antibodies, cytotoxic drugs, or combination)

IT Antibodies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**nonlethal** methods for conditioning recipient for bone marrow **transplant** using **sublethal** doses of total body irradn., cell type-specific antibodies, cytotoxic drugs, or combination)

IT Adipose tissue
(adipocyte, antibody to; **nonlethal** methods for conditioning recipient for bone marrow **transplant** using **sublethal** doses of total body irradn., cell type-specific antibodies, cytotoxic drugs, or combination)

IT Immunoglobulins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antilymphocyte globulins, **nonlethal** methods for conditioning recipient for bone marrow **transplant** using **sublethal** doses of total body irradn., cell type-specific antibodies, cytotoxic drugs, or combination)

IT Therapeutics
(chemo-, antibody-chemotherapeutic agent conjugates; **nonlethal** methods for conditioning recipient for bone marrow **transplant** using **sublethal** doses of total body irradn., cell type-specific antibodies, cytotoxic drugs, or combination)

IT Radioelements, biological studies
Toxins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates, with antibodies; **nonlethal** methods for conditioning recipient for bone marrow **transplant** using **sublethal** doses of total body irradn., cell type-specific antibodies, cytotoxic drugs, or combination)

IT Antibodies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates, with antiproliferative agents; **nonlethal** methods for conditioning recipient for bone marrow **transplant** using **sublethal** doses of total body irradn., cell type-specific antibodies, cytotoxic drugs, or combination)

IT Blood vessel
(endothelium, antibody to bone marrow endothelial cell; **nonlethal** methods for conditioning recipient for bone marrow **transplant** using **sublethal** doses of total body irradn., cell type-specific antibodies, cytotoxic drugs, or combination)

IT Antibodies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal, **nonlethal** methods for conditioning recipient for bone marrow **transplant** using **sublethal** doses of total body irradn., cell type-specific antibodies, cytotoxic drugs, or combination)

IT Bone marrow

(reticular cell, adventitial, antibody to, and to other bone marrow stromal cells; **nonlethal** methods for conditioning recipient for bone marrow **transplant** using **sublethal** doses of total body irradn., antibodies, cytotoxic drugs, or combination)

IT **Hematopoietic precursor cell**
(stem, **nonlethal** methods for conditioning recipient for bone marrow **transplant** using **sublethal** doses of total body irradn., cell type-specific antibodies, cytotoxic drugs, or combination)

IT Bone marrow
(stroma, antibody to bone marrow stromal cell; **nonlethal** methods for conditioning recipient for bone marrow **transplant** using **sublethal** doses of total body irradn., cell type-specific antibodies, cytotoxic drugs, or combination)

IT Bone marrow
(**transplant, nonlethal** methods for conditioning recipient for bone marrow **transplant** using **sublethal** doses of total body irradn., cell type-specific antibodies, cytotoxic drugs, or combination)

IT 50-18-0, Cyclophosphamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**nonlethal** methods for conditioning recipient for bone marrow **transplant** using **sublethal** doses of total body irradn., cell type-specific antibodies, cytotoxic drugs, or combination)

L56 ANSWER 34 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **1996:263792** HCAPLUS
DN **125:52898**
TI Ex vivo expansion of **hematopoietic progenitor cells** for clinical application
AU Arseniev, Lubomir; Battmer, Karin; Stucki, Angelika; Suedmeyer, Ingrid; Kadar, Janos G.; Martin, Michael; Link, Hartmut
CS Abt. Haematol. Onkol, Med. Hochsch. Hannover, Hannover, D-30623, Germany
SO Medizinische Klinik (Munich) (1996), 91(Sondernr. 3), 50-9
CODEN: MEKLA7; ISSN: 0723-5003
PB Urban & Vogel
DT Journal
LA German
CC 9-11 (Biochemical Methods)
Section cross-reference(s): 14
AB G-CSF mobilized and purified CD34+ blood cells of healthy sibling donors and patients with solid tumors were cultured in a 2-mL and 50-mL scale in the presence of the interleukins IL-1.beta., IL-3 and IL-6 (each at a dose of 300 units/mL) and **stem cell** factor (25 ng/mL) without or with erythropoietin (1 unit/mL) for 5 and 4 wk, resp. The nucleated cell counts increased approx. 7-fold and 10-70-fold after 1 and 2 wk, resp. Thereby the nos. of CD34+ cells doubled or tripled without changes in their clonogenicity (CFU-GM and BFU-E output). Thereafter, a depletion of the CD34+ cell pool was noticed. However, the nos. of CD34+/CD38- or CD34+/HLA-DR cells were reduced to a lesser content. The expanded cells generated predominantly myeloid and almost no lymphoid cells. The culture conditions might be feasible for a large-scale ex vivo expansion for clin. application.
ST **hematopoietic progenitor cell** culture **transplant**
IT Animal tissue culture
Hematopoietic precursor cell
Transplant and **Transplantation**
(culture of **hematopoietic precursor cells** for clin. application)

IT Glycophorins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(A, antigen expression during culture of **hematopoietic precursor cells**)
IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**CD33**, antigen expression during culture of **hematopoietic precursor cells**)
IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD34, antigen expression during culture of **hematopoietic precursor cells**)
IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD38, antigen expression during culture of **hematopoietic precursor cells**)
IT Glycoproteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IIIb, antigen expression during culture of **hematopoietic precursor cells**)
IT Lymphokines and Cytokines
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(interleukin 3, culture of **hematopoietic precursor cells** for clin. application)
IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.beta.3, antigen expression during culture of **hematopoietic precursor cells**)
IT 83869-56-1, GM-CSF 143011-72-7, G-CSF
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(culture of **hematopoietic precursor cells** for clin. application)

L56 ANSWER 35 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **1995:975273** HCAPLUS
DN **124:80953**
TI Megadose of T cell-depleted bone marrow overcomes MHC barriers in **sublethally** irradiated mice
AU Bachar-Lustig, Esther; Rachamim, Nurit; Li, Hong-Wei; Lan, Fengshuo; **Reisner, Yair**
CS Dep. of Membrane Research and Biophysics, The Weizmann Inst. of Science, Rehovot, 76100, Israel
SO Nature Medicine (New York) (1995), 1(12), 1268-73
CODEN: NAMEFI; ISSN: 1078-8956
PB Nature Publishing Co.
DT Journal
LA English
CC 8-9 (Radiation Biochemistry)
Section cross-reference(s): 14
AB **Graft**-vs.-host disease (GVHD) is uniformly **lethal** in recipients of HLA-mismatched marrow. In patients with severe combined immunodeficiency disease, this major obstacle can be overcome by rigorous T-cell depletion before **transplantation**. In leukemia patients, however, the benefit of preventing GVHD is offset by **graft rejection** or **graft** failure. Very recently, this problem was overcome by supplementing T cell-depleted bone marrow **transplants** with megadoses of peripheral blood **stem cells** collected by leukapheresis after mobilization of the donor **stem cells** with granulocyte colony-stimulating factor (G-CSF). In the present study, the authors further demonstrate in a mouse

model (C57BL/6.fwdarw.C3H/HeJ) that escalation of bone marrow doses by four- to five fold leads to full donor-type chimerism in **sublethally** irradiated (6.5 Gy) recipients. Thus, the new source of G-CSF mobilized human hematopoietic **stem cells** may enable extending the use of mismatched bone marrow **transplants** to patients with non-malignant diseases for whom **supralethal** conditioning is not a prerequisite.

ST bone marrow **transplant** MHC barrier irradn

IT Gamma ray
Radiotherapy
(megadose of T cell-depleted bone marrow supplemented with G-CSF mobilized **stem cells** overcomes MHC barriers in **sublethally** irradiated mice)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MHC (major histocompatibility complex), megadose of T cell-depleted bone marrow supplemented with G-CSF mobilized **stem cells** overcomes MHC barriers in **sublethally** irradiated mice)

IT Lymphocyte
(T-cell, megadose of T cell-depleted bone marrow supplemented with G-CSF mobilized **stem cells** overcomes MHC barriers in **sublethally** irradiated mice)

IT **Transplant and Transplantation**
(**graft**-vs.-host reaction, megadose of T cell-depleted bone marrow supplemented with G-CSF mobilized **stem cells** overcomes MHC barriers in **sublethally** irradiated mice)

IT **Hematopoietic precursor cell**
(stem, megadose of T cell-depleted bone marrow supplemented with G-CSF mobilized **stem cells** overcomes MHC barriers in **sublethally** irradiated mice)

IT Bone marrow
(**transplant**, megadose of T cell-depleted bone marrow supplemented with G-CSF mobilized **stem cells** overcomes MHC barriers in **sublethally** irradiated mice)

IT 143011-72-7, Granulocyte colony-stimulating factor
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(megadose of T cell-depleted bone marrow supplemented with G-CSF mobilized **stem cells** overcomes MHC barriers in **sublethally** irradiated mice)

L56 ANSWER 36 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **1995:928092** HCAPLUS
TI Hematopoietic **stem cell transplantation** for cancer therapy
AU **Reisner, Yair**; Segall, Harry
CS Weizmann Inst. Sci., Rehovot, Israel
SO Curr. Opin. Immunol. (1995), 7(5), 687-93
CODEN: COPIEL; ISSN: 0952-7915
DT Journal
LA English
AB Bone marrow **transplantation** has become well established in the treatment of malignant disorders. High-dose chemotherapy with hematopoietic **stem cell** support is widely used for most hematol. malignancies, as well as for some solid tumors. In the light of recent developments in **blood progenitor cell** harvest, there have been clin. trials with autologous and **allogeneic transplants**. In part8cular, the availability of large nos. of blood **stem cells**, mobilized by granulocyte colony-stimulating factor and collected by leukapheresis, has made it possible to overcome histocompatibility barriers in HLA-mismatched leukemia patients. Other recent developments include new methods for

blood progenitor cells mobilization and ex vivo expansion, the use of umbilical cord blood as an alternative source of **stem cells**, and mol. techniques that may, in the future, provide other modalities of purging tumor cells from autologous **grafts**.

L56 ANSWER 37 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **1995:792353** HCAPLUS
DN **123:196460**
TI Bone marrow **transplantation** across HLA barriers by increasing the number of **transplanted** cells
AU **Reisner, Yair**; Martelli, Massimo F.
CS Weizmann Institute of Science, Rehovot, 76100, Israel
SO Immunology Today (1995), 16(9), 437-40
CODEN: IMTOD8; ISSN: 0167-4919
PB Elsevier Trends Journals
DT Journal
LA English
CC 15-8 (Immunochemistry)
AB Throughout the 1970s, **graft**-vs.-host disease (GVHD) was uniformly **lethal** in recipients of HLA-mismatched bone marrow. This major obstacle was overcome in 1980 by the introduction of rigorous T-cell depletion prior to **transplantation** into patients with severe combined immunodeficiency. However, in leukemia patients, the benefit of preventing GVHD was offset by **graft rejection** or **graft** failure. In this article, Yair Reisner and Massimo Martelli discuss how this problem may be overcome by intensification of the conditioning protocol in conjunction with a major increase in the dose of **transplanted stem cells**.
ST bone marrow **transplant** HLA antigen
IT Leukemia
(bone marrow **transplantation** across HLA barriers by increasing the no. of **transplanted** cells in)
IT Histocompatibility antigens
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(HLA, bone marrow **transplantation** across HLA barriers by increasing the no. of **transplanted** cells)
IT Bone marrow
(**transplant**, bone marrow **transplantation** across HLA barriers by increasing the no. of **transplanted** cells)

L56 ANSWER 38 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **1995:702154** HCAPLUS
DN **123:81611**
TI Bone marrow **transplantation** from cytokine-treated donor to conditioned recipient
IN **Reisner, Yair**; Martelli, Massimo
PA Yeda Research and Development Co. Ltd., Israel
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K035-12
ICS A61K035-28; A61K038-27
CC 15-5 (Immunochemistry)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9512404	A1	19950511	WO 1994-US12610	19941102
W: AU, CA, JP, NZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9510872	A1	19950523	AU 1995-10872	19941102

PRAI IL 1993-107483 19931103
WO 1994-US12610 19941102

AB A method for bone marrow **transplantation** from an HLA-nonmátched donor to a patient comprises conditioning the patient under a suitable regimen followed by **transplantation** of a very large dose of stem cells which is .gtoreq.3-fold greater than the conventional doses used in T cell-depleted bone marrow **transplantation**. The patient is conditioned under **lethal** or **supralethal** conditions for the treatment of malignant or nonmalignant diseases, or under **sublethal** conditions for the treatment of nonmalignant diseases. The **transplant** may consist of T cell-depleted bone marrow stem cells and T cell-depleted stem cell-enriched peripheral blood mononuclear cells (PBMC) from the HLA-nonmatched donor, preferably a relative of the patient, which donor was previously treated with a drug, e.g. a cytokine such as granulocyte colony-stimulating factor (G-CSF). Thus, recipients received 8 Gy total-body irradn., thiotepa (10 mg/kg in divided doses by infusion), and rabbit anti-human thymocyte globin (5 mg/kg by infusion), and cyclophosphamide (60 mg/kg) prior to **transplantation**. Recombinant human G-CSF (12 .mu.g/kg/day) was infused s.c. into donors for 5-7 days beginning 24 h after bone marrow harvesting, and PBMC were harvested by leukapheresis. The PBMC and bone marrow cells were depleted of T-lymphocytes with soybean agglutinin and E-rosetting. A 7-10-fold increase in the dose of the **transplant** inoculum was achieved by adding T cell-depleted G-CSF-mobilized PBMC to the T cell-depleted bone marrow. Prompt and sustained **engraftment** was obsd. in 16 of 17 recipients of haploidentical mismatched T cell-depleted bone marrow. **Graft**-vs.-host disease owing to T-cell contamination of the PBMC was seen in only 1 case.

ST bone marrow **transplant** colony stimulating factor; HLA mismatched bone marrow **transplant**; mononuclear leukocyte bone marrow **transplant** HLA

IT Bone marrow
Gaucher's disease
Neoplasm
Thalassemia
Transplant and **Transplantation**
(bone marrow **transplantation** from cytokine-treated donor to conditioned recipient)

IT Agglutinins and Lectins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(soybean; bone marrow **transplantation** from cytokine-treated donor to conditioned recipient)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HLA, bone marrow **transplantation** from cytokine-treated donor to conditioned recipient)

IT Leukemia
(acute lymphoblastic, bone marrow **transplantation** from cytokine-treated donor to conditioned recipient)

IT Leukemia
(acute myelogenous, bone marrow **transplantation** from cytokine-treated donor to conditioned recipient)

IT Anemia (disease)
(aplastic, bone marrow **transplantation** from cytokine-treated donor to conditioned recipient)

IT Leukemia
(chronic myelocytic, bone marrow **transplantation** from cytokine-treated donor to conditioned recipient)

IT Hematopoiesis
(disorder, bone marrow **transplantation** from cytokine-treated donor to conditioned recipient)

IT Bone, disease
(osteopetrosis, bone marrow **transplantation** from cytokine-treated donor to conditioned recipient)
IT Immunodeficiency
(severe combined, bone marrow **transplantation** from cytokine-treated donor to conditioned recipient)
IT Hematopoietic precursor cell
(stem, bone marrow **transplantation** from cytokine-treated donor to conditioned recipient)
IT 143011-72-7, Granulocyte colony-stimulating factor
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bone marrow **transplantation** from cytokine-treated donor to conditioned recipient)

L56 ANSWER 39 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **1995:499199** HCAPLUS
DN **122:261992**
TI A unique population of CD34+ cells in cord blood
AU Nimgaonkar, Maya T.; Roscoe, Rochelle A.; Persichetti, Jeannette; Rybka, Witold B.; Winkelstein, Alan; Ball, Edward D.
CS School of Medicine, University of Pittsburgh, Pittsburgh, PA, USA
SO Stem Cells (Miamisburg, OH, United States) (1995), 13(2), 158-66
CODEN: STCEEJ; ISSN: 1066-5099
DT Journal
LA English
CC 13-5 (Mammalian Biochemistry)
AB Human umbilical cord blood (CB) is a rich source of hematopoietic **stem cells** for both research and **stem cell transplantation**. In clin. studies, it appears that recovery from myeloablative therapy using CB requires significantly fewer cells than a typical **allogeneic** marrow **transplant**. This suggests that CB may be enriched for early hematopoietic progenitors. The present studies were undertaken to det. the presence of CD34+ cells in CB with the phenotypic characteristics of multipotential **stem cells**. In 22 CB harvests, the av. percentage of CD34+ cells was 1.33%, a value similar to that in adult normal bone marrows (BM). However, the distribution of CD34+ cells was distinctly different from either BM or granulocyte colony-stimulating factor (G-CSF) mobilized peripheral blood **stem cell** harvests. CB contained a defined population of brightly staining CD34+ cells with low side scatter. These CD34 (bright) cells comprised a mean of 14.5% of the CB CD34+ cells, whereas <1% of BM CD34+ cells has been shown to be CD34-bright. Eighty-five to ninety percent were neg. for three antigens expressed at an early stage of **stem cell** maturation: CD38, HLA-DR and LFA-1. Fifty-five percent of these CD34 (bright) cells did not express the CD45RA isoform, an addnl. marker of immaturity. The antigen-bright cells also lacked lineage-specific antigens including **CD33**, CD56, CD19, CD10 and CD7 as well as CD71. Approx. 46% were Thy-1+, and 40% expressed c-kit receptors. These data suggest that, by phenotypic criteria, CB may be a particularly enriched source of primitive hematopoietic precursors.
ST hematopoietic **stem cell** CD34 cord blood
IT Newborn
(unique population of CD34+ cells in human cord blood)
IT **Hematopoietic precursor cell**
(stem, unique population of CD34+ cells in human cord blood)

L56 ANSWER 40 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN 1995:328637 HCAPLUS
DN 122:103949
TI Surrogate tolerogenesis for the development of **tolerance** to

xenografts
IN Beschorner, William E.
PA Johns Hopkins University, USA
SO PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K035-00
ICS C12N005-00
CC 15-10 (Immunochemistry)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9427622	A1	19941208	WO 1994-US5844	19940524
	W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9470445	A1	19941220	AU 1994-70445	19940524
	EP 700297	A1	19960313	EP 1994-919227	19940524
	EP 700297	B1	20020731		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 09500618	T2	19970121	JP 1994-500907	19940524
	AT 221382	E	20020815	AT 1994-919227	19940524
	US 6060049	A	20000509	US 1995-295899	19950606
PRAI	US 1993-65370	A	19930524		
	WO 1994-US5844	W	19940524		

AB This invention provides a method for developing immune **tolerance** in xenogeneic organ **graft** recipients, in which lymphohematopoietic cells from an intended organ **graft** recipient are differentiated within a xenogeneic surrogate, such as a fetal animal. After birth of the surrogate, the matured lympho-**hematopoietic cells** contg. antigen specific regulatory cells, including suppressor cells, **veto** cells, select B cells, anti-idiotype antibodies, and other related factors responsible for antigen specific **tolerance** in a surrogate animal are reintroduced into the intended organ **graft** recipient, in conjunction with an organ **transplant** or a tissue **transplant** from the **xenograft** surrogate. The invention also provides an organ **graft** repopulated with cells from the intended organ **graft** recipient produced in a surrogate animal. In example, peripheral blood fraction contg. lymphocytes and antigen-presenting cells were sepd., incubated with growth factors, and introduced into fetal pigs in pregnant sow during the first or second trimester. Two months after birth, most optimal surrogate pig was chosen for organ **transplant**.

ST **xenograft transplant** surrogate tolerogenesis
IT Animal cell
(anti-idiotype antibody-producing; surrogate tolerogenesis for the development of **tolerance** to **xenografts**)
IT Antibodies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(immunosuppressive; surrogate tolerogenesis for the development of **tolerance** to **xenografts**)
IT Monocyte
(organ **transplant**; surrogate tolerogenesis for the development of **tolerance** to **xenografts**)
IT Immune **tolerance**
Immunological accessory cell
Lymphocyte
(surrogate tolerogenesis for the development of **tolerance** to **xenografts**)
IT Burn

(surrogate tolerogenesis for the development of **tolerance** to **xenografts** for treating burn or fulminant hepatitis or hepatitis necrosis)
IT Lymphocyte
(T-cell, suppressor cell, surrogate tolerogenesis for the development of **tolerance** to **xenografts**)
IT Leukocyte
(dendritic cell, organ **transplant**; surrogate tolerogenesis for the development of **tolerance** to **xenografts**)
IT Blood vessel
(endothelium, organ **transplant**; surrogate tolerogenesis for the development of **tolerance** to **xenografts**)
IT Hepatitis
(fulminant, surrogate tolerogenesis for the development of **tolerance** to **xenografts** for treating burn or fulminant hepatitis or hepatitis necrosis)
IT Liver
(hepatocyte, **transplant**; surrogate tolerogenesis for the development of **tolerance** to **xenografts**)
IT **Hematopoietic precursor cell**
(lymphoid, surrogate tolerogenesis for the development of **tolerance** to **xenografts**)
IT Liver, disease
(necrosis, surrogate tolerogenesis for the development of **tolerance** to **xenografts** for treating burn or fulminant hepatitis or hepatic necrosis)
IT Lymphocyte
(suppressor cell, **veto**, surrogate tolerogenesis for the development of **tolerance** to **xenografts**)
IT Bone marrow
Pancreatic islet of Langerhans
(**transplant**, surrogate tolerogenesis for the development of **tolerance** to **xenografts**)
IT **Transplant** and **Transplantation**
(xeno-, **transplant**; surrogate tolerogenesis for the development of **tolerance** to **xenografts**)

L56 ANSWER 41 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN 1994:407245 HCAPLUS
DN 121:7245
TI A role for transforming growth factor-beta in the **veto** mechanism in **transplant tolerance**
AU Verbanac, Kathryn M.; Carver, F. Melinda; Haisch, Carl E.; Thomas, Judith M.
CS Dep. Surg., East Carol. Univ. Sch. Med., Greenville, NC, 27858, USA
SO Transplantation (1994), 57(6), 893-900
CODEN: TRPLAU; ISSN: 0041-1337
DT Journal
LA English
CC 15-10 (Immunochemistry)
AB The authors have studied the **veto** cell-mediated induction of **transplant tolerance** by **allogeneic** donor bone marrow cells and have achieved kidney **allograft tolerance** in a preclin. rhesus monkey model. Here the authors extend these studies to investigate the **veto** mechanism of CTLp suppression and the role of CD8 and TGF-.beta. in these events. Infusion of DR-/dim donor BMC into RATG-treated rhesus monkeys induced functional deletion of donor-specific CTLp and prolongation of kidney **allograft** survival, whereas depletion of the CD8+ subset from BMC ablated these effects. A role of CD8 in the **veto** effect was further implicated by rhesus MLR-induced CML expts. in which pretreatment of normal responder cells with MAb to MHC class I, the natural ligand of CD8, blocked the suppressive activity of **allogeneic** BMC. In

addn., pretreatment of the BMC with anti-CD8 MAbs blocked strong **veto** activity significantly, suggesting that CD8 functions as an accessory or adhesion ligand. In contrast, anti-CD8 treatment significantly **enhanced** weak BMC-mediated **veto** activity, suggesting that CD8 might addnl. serve as a signal transducer to increase **veto** activity, perhaps by the induction of cytokine release. The cytokine TGF-.beta. was studied because it has immunosuppressive properties that are shared by **veto** cells. Human TGF-.beta., like BMC **veto** cells, inhibited MLR-induced CML in a dose-dependent manner, and anti-TGF-.beta. Ig relieved the BMC-mediated **veto** suppressive effect. Active TGF-.beta. was detected only in the supernatants of CML cultures contg. BMC. Pretreatment of BMC with L-leucyl-leucine Me ester (Leu-leu-OMe), which eliminates cytotoxic precursor and effector lymphocytes and monocytes, did not affect levels of active TGF-.beta.. In previous studies, the **veto** effect of BMC was also shown to be Leu-leu-OMe-resistant. Finally, treatment of isolated DR-/dim BMC cultures with anti-CD8 elicited TGF-.beta. secretion, whereas anti-CD2 or anti-CD3 had no effect. When isolated after stimulation with anti-CD8, only the CD8+ subset of DR-/dim BMC produced detectable levels of active TGF-.beta.. In summary, these studies demonstrate that CD8 functions as an immunoregulatory mol. in **veto** effects by freshly isolated rhesus BMC and suggest that CD8-ligand interactions may induce low-level secretion of TGF-.beta. to mediate or facilitate the **veto** mechanism of CTLp inactivation in a paracrine manner.

ST kidney **allograft tolerance** transforming growth factor

IT **Immune tolerance**
(to kidney **allografts**, transforming growth factor-.beta. in)

IT **Transplant and Transplantation**
(allo-, of kidney, rejection of, resistance to, transforming growth factor-.beta. in)

IT Kidney
(**allotransplant, tolerance** to, transforming growth factor-.beta. in)

IT **Hematopoietic precursor cell**
(cytotoxic T-cell, transforming growth factor-.beta. in kidney **allograft tolerance** in relation to)

IT Animal growth regulators
RL: BIOL (Biological study)
(.beta.-transforming growth factors, in kidney **allograft tolerance**)

L56 ANSWER 42 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN 1994:242175 HCAPLUS
DN 120:242175
TI Potential use of interleukin-6 in bone marrow **transplantation**: effects of recombinant human interleukin-6 after syngeneic and **semiallogeneic** bone marrow **transplantation** in mice
AU Givon, Tamar; Revel, Michel; Slavin, Shimon
CS Dep. Bone Marrow Transplant., Hadassah Univ. Hosp., Jerusalem, 91120, Israel
SO Blood (1994), 83(6), 1690-7
CODEN: BLOOAW; ISSN: 0006-4971
DT Journal
LA English
CC 15-5 (Immunochemistry)
AB The potential of recombinant glycosylated human interleukin-6 (rhIL-6) for **enhancing** immunohematopoietic reconstitution and survival after syngeneic and **semiallogeneic** bone marrow **transplantation** (BMT) in BALB/c mice subjected to total body irradn. (TBI) was investigated. RhIL-6 produced **enhanced** reconstitution of white blood cells as assessed on days 8 and 14 after syngeneic BMT and of platelets as assessed on day 10. Moreover, rhIL-6 treatment produced

significant improvement of survival in **lethally** irradiated mice receiving either syngeneic or **semiallogeneic** BMT with limiting no. of BM cells. This effect of IL-6 was not seen with large BM cell inocula producing high survival by themselves. RhIL-6 showed no toxic effects and did not affect the survival of mice that were **lethally** irradiated but not reconstituted by BM cells. However, the sensitivity of mice to **sublethal** irradn. was increased by rhIL-6 in the absence of BM cell **transplantation**. In exptl. conditions inducing **graft**-vs.-host disease (GVHD), in which **lethally** irradiated (BALB/c .times. C57BL/6)F1 mice received mixts. of BM and spleen cells from C57BL/6 donors, rhIL-6 was found to **enhance** GVHD manifestations. No consistent **enhancement** of T-cell in vitro proliferative responses to **allogeneic** spleen cells or T- and B-cell-dependent mitogens were seen in the splenocytes obtained from recipients of syngeneic or **semiallogeneic** BMT. The data suggest that rhIL-6 may be useful in BMT procedures to **enhance** thrombopoiesis and hematol. recovery, as well as to increase overall survival rates. In addn., the potentiation of GVHD, which is considered to correlate with **graft**-vs.-leukemia effects, may be of interest in **enhancing** GVHD-dependent antitumor effects in protocols combining radiochemotherapy with BMT.

ST **transplantation** bone marrow interleukin 6

IT **Hematopoietic precursor cell**
(syngeneic and **semiallogeneic transplantation** of, interleukin-6 effect on)

IT **Transplant and Transplantation**
(syngeneic and **semiallogeneic**, of bone marrow, interleukin-6 effect on)

IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(interleukin 6, syngeneic and **semiallogeneic** bone marrow **transplantation** response to)

L56 ANSWER 43 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **1993:492290** HCAPLUS
DN **119:92290**
TI Chimeric mammals with human **hematopoietic cells**
IN Dick, John E.; Williams, Douglas E.; Lapidot, Tsvee
PA Immunex Corp., USA
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K035-00
ICS C12N005-00; C07K013-00
CC 13-1 (Mammalian Biochemistry)
Section cross-reference(s): 9, 15
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9309792	A1	19930527	WO 1992-US9913	19921119
	W: AU, CA, FI, JP, NO				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
	US 6353150	B1	20020305	US 1991-797493	19911122
	AU 9331781	A1	19930615	AU 1993-31781	19921119
	EP 625907	A1	19941130	EP 1993-900531	19921119
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
PRAI	US 1991-797493	A	19911122		
	WO 1992-US9913	A	19921119		

AB A chimeric mammal is disclosed which has a stable bone marrow **graft** of human **hematopoietic cells** capable of differentiating into multiple lineages of human mature cells, wherein .gtoreq.30% of the **hematopoietic cells** in the mammal's

bone marrow are of human origin. The method comprises **sublethally** irradiating an immunodeficient mammal, infusing human **hematopoietic cells** into the mammal, and administering an effective amt. of human mast cell growth factor and a human GM-CSF/interleukin-3 fusion protein to promote **engraftment** of human cells within the chimeric mammal's bone marrow. The method was demonstrated in SCID (severe combined immune deficiency) mice.

ST chimeric mammal human **hematopoietic cell**; mouse chimeric human **hematopoietic cell**; SCID mouse human **hematopoietic cell**

IT Glycophorins
RL: BIOL (Biological study)
(chimeric SCID mouse with human **hematopoietic cells** in relation to cells pos. for)

IT **Hematopoietic precursor cell**
(chimeric mammal with **graft** of, of human)

IT Hybridoma
(chimeric mammal with human **hematopoietic cells** for immunization in prodn. of)

IT **Hematopoietic precursor cell**
(chimeric mammal with, of human)

IT Erythrocyte
(chimeric mouse with **hematopoietic cells** of human for prodn. of)

IT Mouse
(chimeric, with **hematopoietic cells** of human)

IT Mammal
(chimeric, with human **hematopoietic cells**)

IT **Transplant** and **Transplantation**
(of human **hematopoietic cells** into immunodeficient mammal)

IT Lymphocyte
(B-cell, immunodeficient mammal lacking functional, for prodn. of chimeric mammal with **hematopoietic cells** of human)

IT Antigens
RL: BIOL (Biological study)
(CD19, chimeric SCID mouse with human **hematopoietic cells** in relation to cells pos. for)

IT Antigens
RL: BIOL (Biological study)
(**CD33**, chimeric SCID mouse with human **hematopoietic cells** in relation to cells pos. for)

IT Antigens
RL: BIOL (Biological study)
(CD34, chimeric SCID mouse with human **hematopoietic cells** in relation to cells pos. for)

IT Immunoglobulins
RL: PREP (Preparation)
(G, prodn. of, of human, in chimeric mouse with human **hematopoietic cells**)

IT Immunoglobulins
RL: PREP (Preparation)
(M, prodn. of, of human, in chimeric mouse with human **hematopoietic cells**)

IT Lymphocyte
(T-cell, immunodeficient mammal lacking functional, for prodn. of chimeric mammal with **hematopoietic cells** of human)

IT **Hematopoietic precursor cell**
(erythroid, chimeric mammal with **graft** of, of human)

IT **Hematopoietic precursor cell**
(erythroid burst-forming, chimeric SCID mouse with human **hematopoietic cells** in relation to prodn. of)

IT **Hematopoietic precursor cell**

(granulocyte-macrophage colony-forming, chimeric SCID mouse with human **hematopoietic cells** in relation to prodn. of)
IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(interleukin 2, in chimeric mammal prodn. with **hematopoietic cells** of human)
IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(interleukin 3, fusion protein with GM-CSF, in chimeric mammal prodn. with **hematopoietic cells** of human)
IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(interleukin 4, in chimeric mammal prodn. with **hematopoietic cells** of human)
IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(interleukin 5, in chimeric mammal prodn. with **hematopoietic cells** of human)
IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(interleukin 6, in chimeric mammal prodn. with **hematopoietic cells** of human)
IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(interleukin 7, in chimeric mammal prodn. with **hematopoietic cells** of human)
IT **Hematopoietic precursor cell**
(lymphoid, chimeric mammal with **graft** of, of human)
IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(mast cell growth factor, in chimeric mammal prodn. with **hematopoietic cells** of human)
IT Antibodies
RL: BIOL (Biological study)
(monoclonal, hybridoma producing, chimeric mammal with human **hematopoietic cells** for immunization in prodn. of)
IT **Hematopoietic precursor cell**
(myeloid, chimeric mammal with **graft** of, of human)
IT Immunodeficiency
(severe combined, mouse with, in chimeric mammal prodn. with **hematopoietic cells** of human)
IT 9054-63-1
RL: BIOL (Biological study)
(chimeric SCID mouse with human **hematopoietic cells** in relation to cells pos. for)
IT 11096-26-7, Erythropoietin 83869-56-1, GM-CSF 83869-56-1D, GM-CSF, interleukin-3 fusion products 143011-72-7, G-CSF
RL: BIOL (Biological study)
(in chimeric mammal prodn. with **hematopoietic cells** of human)

L56 ANSWER 44 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **1993:52415** HCAPLUS
DN **118:52415**
TI Durable **engraftment** of human tissue and cells in normal mammals
IN **Reisner, Yair**
PA Yeda Research and Development Co., Ltd., Israel
SO Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM C12N015-00
ICS G01N033-574; A01K067-027

CC 1-1 (Pharmacology)
Section cross-reference(s): 14, 15
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 517199	A1	19921209	EP 1992-109402	19920603
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE				
	JP 05227861	A2	19930907	JP 1992-144568	19920604
	US 5709843	A	19980120	US 1994-347088	19941123
PRAI	IL 1991-98369	A	19910604		

AB A nonhuman chimeric mammal M4, having tissue or cells other than normal **hematopoietic cells** originating from a mammal M3 (e.g. human malignant cells derived from leukemia or solid tumor cells or tissue of human organs), is prepd. from a mammal M1 whose **hematopoietic cells** have been substantially suppressed or destroyed and replaced by **hematopoietic cells** originating form a mammal M2, of a species other than that of M3, having a genetically-detd. hematopoietic deficiency, and to which mammal M1 tissue or cells of mammal M3 have been **transplanted**. The chimeric mammal M4 is prepd. by treating nonhuman mammal M1 to essentially destroy its immune system; **transplantng** the treated mammal M1 with tissue or cells other than normal **hematopoietic cells** from mammal M3; and addnl. **transplanting** with **hematopoietic cells** from mammal M2, of a species other than that of M3, having a genetically-detd. hematopoietic deficiency. A method for chemotherapy sensitivity testing of a drug against a human solid tumor or leukemia comprises treating a chimeric mammal prepd. as above with the drug, and monitoring the efficacy of the treatment. Female BALB/c mice were irradiated to destroy the immune system and then **transplanted** 1 day later with human melanoma cells. Twenty-four h later, T-cell-depleted bone marrow cells from SCID mice were **transplanted** into the treated mice by i.v. infusion. Ten of 12 **grafted** mice that survived the treatments developed primary tumors. Spontaneous metastasis was obsd. in 2 of the 10.

ST chemotherapy testing mammal neoplasm **transplant**; hematopoiesis deficiency mammal neoplasm **transplant**; drug analysis leukemia **transplant** hematopoiesis deficiency

IT Kidney, neoplasm
Leukemia
Lung, neoplasm
Melanoma
Ovary, neoplasm
Pancreas, neoplasm
Stomach, neoplasm
(cells, **transplant**, of human into immunodeficient nonhuman mammal also **transplanted** with **hematopoietic cells** of nonhuman mammal having genetically-detd. hematopoietic deficiency, chemotherapy sensitivity testing in relation to)

IT **Hematopoietic precursor cell**
(chimeric nonhuman mammal with **transplanted** tissue of human organs or human leukemia or solid tumor cells and with nonhuman deficient, chemotherapy sensitivity testing in relation to)

IT Mammal
(chimeric nonhuman, with **transplanted** hematopoietic deficient cells of nonhuman and **transplanted** tissue of human organs or human leukemia or solid tumor cells, chemotherapy sensitivity testing in relation to)

IT Mouse
(chimeric, with **transplanted** hematopoietic deficient cells of nonhuman and **transplanted** tissue of human organs or human leukemia or solid tumor cells, chemotherapy sensitivity testing in relation to)

IT Immunodeficiency

(mouse with, hematopoietic deficient cells of nonhuman and tissue of human organs or human leukemia or solid tumor cells **transplantation** into, chemotherapy sensitivity testing in relation to)

IT Immunity
(nonhuman mammal with destroyed, hematopoietic deficient cells of nonhuman and tissue of human organs or human leukemia or solid tumor cells **transplantation** into, chemotherapy sensitivity testing in relation to)

IT Lymph node
(of human into immunodeficient nonhuman mammal also **transplanted** with **hematopoietic cells** of nonhuman mammal having genetically-detd. hematopoietic deficiency, chemotherapy sensitivity testing in relation to)

IT **Transplant and Transplantation**
(of tissue of human organs or human leukemia or solid tumor cells into immunodeficient mammal also **transplanted** with **hematopoietic cells** of nonhuman mammal having genetically-detd. hematopoietic deficiency, chemotherapy screening in relation to)

IT Pharmaceutical analysis
(sensitivity testing in, in chimeric nonhuman mammal having **transplanted** human organs or human leukemia or solid tumor cells and **transplanted** hematopoietic deficient cells of nonhuman)

IT Neoplasm inhibitors
(sensitivity testing of, in chimeric nonhuman mammal having **transplanted** human organs or human leukemia or solid tumor cells and **transplanted** hematopoietic deficient cells of nonhuman)

IT Leukemia
(acute myelogenous, cells, **transplant**, of human into immunodeficient nonhuman mammal also **transplanted** with **hematopoietic cells** of nonhuman mammal having genetically-detd. hematopoietic deficiency, chemotherapy sensitivity testing in relation to)

IT Therapeutics
(chemo-, drugs for, sensitivity testing of, in chimeric nonhuman mammal having **transplanted** human organs or human leukemia or solid tumor cells and **transplanted** hematopoietic deficient cells of nonhuman)

IT Leukemia
(chronic myelocytic, cells, **transplant**, of human into immunodeficient nonhuman mammal also **transplanted** with **hematopoietic cells** of nonhuman mammal having genetically-detd. hematopoietic deficiency, chemotherapy sensitivity testing in relation to)

IT Intestine, neoplasm
(colon, cells, **transplant**, of human into immunodeficient nonhuman mammal also **transplanted** with **hematopoietic cells** of nonhuman mammal having genetically-detd. hematopoietic deficiency, chemotherapy sensitivity testing in relation to)

IT Hematopoiesis
(disorder, deficiency, chimeric nonhuman mammal with **transplanted** tissue of human organs or human leukemia or solid tumor cells and with nonhuman **hematopoietic cells** of)

IT Leukemia
(lymphocytic, cells, **transplant**, of human into immunodeficient nonhuman mammal also **transplanted** with **hematopoietic cells** of nonhuman mammal having genetically-detd. hematopoietic deficiency, chemotherapy sensitivity testing in relation to)

IT Leukemia
(monocytic, cells, **transplant**, of human into immunodeficient nonhuman mammal also **transplanted** with **hematopoietic cells** of nonhuman mammal having genetically-detd. hematopoietic deficiency, chemotherapy sensitivity testing in relation to)
IT Mammary gland
Prostate gland
(neoplasm, cells, **transplant**, of human into immunodeficient nonhuman mammal also **transplanted** with **hematopoietic cells** of nonhuman mammal having genetically-detd. hematopoietic deficiency, chemotherapy sensitivity testing in relation to)
IT Neuroglia
(neoplasm, glioblastoma, cells, **transplant**, of human into immunodeficient nonhuman mammal also **transplanted** with **hematopoietic cells** of nonhuman mammal having genetically-detd. hematopoietic deficiency, chemotherapy sensitivity testing in relation to)
IT Nerve, neoplasm
(neuroblastoma, cells, **transplant**, of human into immunodeficient nonhuman mammal also **transplanted** with **hematopoietic cells** of nonhuman mammal having genetically-detd. hematopoietic deficiency, chemotherapy sensitivity testing in relation to)
IT Immunodeficiency
(severe combined, T-cell-depleted bone marrow cells of mouse with, chimeric immunodeficient nonhuman mammal **transplanted** with tissue of human organs or human leukemia or solid tumor cells and with, chemotherapy sensitivity testing in relation to)
IT Neoplasm
(solid, cells of, **transplant**, of human into immunodeficient nonhuman mammal also **transplanted** with **hematopoietic cells** of nonhuman mammal having genetically-detd. hematopoietic deficiency, chemotherapy sensitivity testing in relation to)
IT Bone marrow
(**transplant**, of T-cell-depleted severe combined immunodeficiency mouse, into immunodeficient nonhuman mammal also **transplanted** with tissue of human organs or human leukemia or solid tumor cells, chemotherapy sensitivity testing in relation to)
IT Liver
Organ
Pancreas
Spleen
Thymus gland
(**transplant**, splanted*** with **hematopoietic cells** of **nonhuman mammal having genetically-detd. hematopoietic** deficiency, chemotherapy sensitivity testing in relation to**Organ** LROLEPancreasROLES ASSIGNSpleenESROLES ASSIGN)

L56 ANSWER 45 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN 1992:2883 HCAPLUS
DN 116:2883
TI The influence of human recombinant interleukin-1.beta. on the repopulation of bone marrow CFU-S of mice subjected to irradiation and burn
AU Alekseeva, L. V.; Izotova, N. I.; Ketlinskii, S. A.; Pereverzev, A. E.; Simbirtsev, A. S.
CS Inst. Cytol., Leningrad, USSR
SO Tsitologiya (1991), 33(3), 88-94
CODEN: TSITAQ; ISSN: 0041-3771
DT Journal
LA Russian
CC 8-6 (Radiation Biochemistry)
AB The radioprotective and restorative (therapeutic) effects of human

recombinant interleukin-1.beta. (IL-1.beta.) were investigated on the population of bone marrow CFU-S of mice, subjected to either **sublethal** doses of x-rays alone or in combination with thermal burn. IL1.beta. was effective both in vitro and in vivo in semisyngeneic, syngeneic, and **allogeneic** animals. If the irradn. was combined with thermal burn, the therapeutic effect of the agent was demonstrated at an irradn. dose equal to 3.06 Gy rather than 6.12 Gy. If the bone marrow cells were irradiated in vitro at 3.06 Gy followed by heat shock at 42.degree. for 10-20 min, the therapeutic effect of IL-1.beta. was seen only if it was added to cells before rather than after irradn. The radioprotective effect of IL-1.beta. was maintained under in vitro as well as in vivo conditions in the **allogeneic** system of **transplantation** of the CBA donor bone marrow in C57BL mice.

ST interleukin hematopoietic precursor x ray burn; radioprotection hematopoiesis interleukin 1beta

IT Burn
(**hematopoietic precursor cells** of bone marrow response to x-rays and, interleukin 1.beta. antagonism of)

IT Radioprotectants
(interleukin 1.beta., of **hematopoietic precursor cells** of bone marrow from x-rays, burn in relation to)

IT X-ray
(protection against, of **hematopoietic precursor cells** of bone marrow by interleukin 1.beta., burn in relation to)

IT Hematopoiesis
(x-ray and burn effect on, by bone marrow, interleukin 1.beta. antagonism of)

IT **Transplant and Transplantation**
(allo-, of bone marrow, interleukin 1.beta. radioprotection in)

IT Bone marrow
(**allotransplant**, interleukin 1.beta. radioprotection in)

IT **Hematopoietic precursor cell**
(colony-forming unit-spleen, x-ray and burn effect on, of bone marrow, interleukin 1.beta. antagonism of)

IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(interleukin 1.beta., x-ray and burn effect on **hematopoietic precursor cells** of bone marrow antagonism by)

L56 ANSWER 46 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN **1991:533995** HCAPLUS
DN **115:133995**
TI Durable **engraftment** and development of human hematopoietic lineages in normal mammals for production of monoclonal antibodies
IN **Reisner, Yair**
PA Yeda Research and Development Co., Ltd., Israel
SO Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM C12N015-00
ICS C12P021-08
CC 15-3 (Immunochemistry)
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 438053	A1	19910724	EP 1991-100047	19910102
	EP 438053	B1	19990616		
	R: CH, DE, DK, FR, GB, IT, LI, NL, SE				
	IL 93067	A1	19951231	IL 1990-93067	19900115
	IL 97128	A1	20001206	IL 1991-97128	19910201
	JP 04267830	A2	19920924	JP 1991-309255	19911125

JP 2647292 B2 19970827
PRAI IL 1990-93067 A 19900115
US 1990-618303 A 19901126

AB A non-human chimeric mammal M4 having long-term stable xenogeneic **hematopoietic cells**, is obtained by doubly **transplanting** a mammal M1, the **hematopoietic cells** of which have been substantially suppressed or destroyed, with **hematopoietic cells** from at least two different sources, at least one of these sources being **hematopoietic cells** originating in a mammal M3 of a species other than that of mammal M1, preferably human, and at least a second of these sources being **hematopoietic cells** originating from a mammal M2, of a species other than that of M3, preferably of the same species as M1, having a genetically-detd. hematopoietic deficiency. In particular, a chimeric mouse having long term stable human B and T cells was obtained by double **engraftment** of human bone marrow cells and of bone marrow cells derived from a mouse with severe combined immunodeficiency. The chimeric mammals may be used for the prodn. of human monoclonal antibodies.

ST monoclonal antibody chimeric mammal; xenogeneic **hematopoietic cell** chimeric mammal

IT Bone marrow
Liver
Lymph gland
Thyme
(chimeric mammal with human cells of, human monoclonal antibody prodn. in relation to)

IT Blood corpuscle
Leukocyte
(chimeric mammal with human, human monoclonal antibody prodn. in relation to)

IT Mouse
(chimeric, human **hematopoietic cells** in, human monoclonal antibody prodn. in relation to)

IT Mammal
(chimeric, with xenogeneic **hematopoietic cells**, human monoclonal antibody prodn. in relation to)

IT **Transplant and Transplantation, animal**
(of xenogeneic **hematopoietic cells** into chimeric mammal, human monoclonal antibody prodn. in relation to)

IT **Hematopoietic precursor cell**
(xenogeneic, chimeric mammal with, human monoclonal antibody prodn. in relation to)

IT Lymphocyte
(B-, chimeric mammal with human, human monoclonal antibody prodn. in relation to)

IT Lymphocyte
(T-, chimeric mammal with human, human monoclonal antibody prodn. in relation to)

IT **Hematopoietic precursor cell**
(erythroid, chimeric mammal with human, human monoclonal antibody prodn. in relation to)

IT Antibodies
RL: BIOL (Biological study)
(monoclonal, manuf. of human, chimeric mammal with human **hematopoietic cells** for)

IT **Hematopoietic precursor cell**
(myeloid, chimeric mammal with human, human monoclonal antibody prodn. in relation to)

IT Immunodeficiency
(severe combined, mouse with, **hematopoietic cells** of, chimeric mammal contg., human monoclonal antibody prodn. in relation to)

IT **Hematopoietic precursor cell**
(stem, chimeric mouse contg. human, human monoclonal antibody prodn. in relation to)

L56 ANSWER 47 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN 1990:530566 HCAPLUS
DN 113:130566
TI Induction of peripheral **tolerance** to class I major histocompatibility complex (MHC) alloantigens in adult mice: transfused class I MHC-incompatible splenocytes **veto** clonal responses of antigen-reactive Lyt-2+ T cells
AU Heeg, Klaus; Wagner, Hermann
CS Inst. Med. Microbiol. Hyg., Tech. Univ. Munich, Munich, D-8000, Germany
SO Journal of Experimental Medicine (1990), 172(3), 719-28
CODEN: JEMEAV; ISSN: 0022-1007
DT Journal
LA English
CC 15-10 (Immunochemistry)
AB The efficacy and the mode of action of **pretransplant** transfusion with class I major histocompatibility complex (MHC)-disparate splenocytes in establishing a state of peripheral **tolerance** in adult mice is analyzed. Adult mice injected i.v. with a crit. no. of .apprx.5 .times. 107 **allogenic** splenocytes accept skin **grafts** and develop chimerism in the peripheral lymphatic tissues, but not in thymus and bone marrow. In parallel, a split **tolerance** evolves: the frequency of class I MHC-reactive Lyt-2+ cytotoxic T lymphocyte precursor (CTL-p)- and interleukin 2 (IL-2)-producing T cells falls off in the peripheral lymphoid tissue, but remains unaltered intrathymically. In particular, high affinity CTL-p become clonally undetectable. In vivo generation of **tolerant** cells is cyclosporin A resistant, but dependent on recipient L3T4+ T cells. Loss of Lyt-2+ CTL-p- and IL-2-producing T cell precursors is not due to active suppression, but is caused by clonal anergy. Donor-derived chimeric cells pos. selected 7 d after i.v. transfusion exhibit in vitro the hallmarks of **veto** cells, i.e., paralyze CTL-p reactive to donor-type class I MHC alloantigens. Apparently, the peripheral (split) **tolerance** induced in vivo by **pretransplant** transfusion operates because donor-type cells develop in vivo efficiently into **veto** cells, which in turn induce a state of clonal anergy within antigen-reactive Lyt-2+ T lymphocytes.
ST transfusion splenocyte antigen incompatible **tolerance**
IT **Immune tolerance**
(peripheral, to class I antigen, to transfused incompatible splenocytes, **veto** cells effect in)
IT **Hematopoietic precursor cell**
(cytotoxic T-lymphocyte, frequency of, in class I antigen **tolerance** induction)
IT Antigens
RL: BIOL (Biological study)
(histocompatibility, class I, induction of peripheral **tolerance** to, from transfused incompatible splenocytes, **veto** cells effect in)
IT Lymphokines and Cytokines
RL: FORM (Formation, nonpreparative)
(interleukin 2, formation of, by T-cells, in peripheral **tolerance** induction)
IT Spleen
(splenocyte, transfused incompatible, induction of peripheral **tolerance** to class I antigen of, **veto** cells in)
IT Lymphocyte
(suppressor, **veto**, in peripheral **tolerance** induction, to class I antigens, from transfused incompatible splenocytes)

IT 59865-13-3, Cyclosporin A
RL: BIOL (Biological study)
(**tolerance** to class I antigens response to, from transfused incompatible splenocytes)

L56 ANSWER 48 OF 48 HCAPLUS COPYRIGHT 2002 ACS
AN 1988:504387 HCAPLUS
DN 109:104387
TI Prevention of **graft**-versus-host disease by treatment of bone marrow with gliotoxin in fully **allogeneic** chimeras and their cytotoxic T cell repertoire
AU Mullbacher, Arno; Moreland, Alvin F.; Waring, Paul; Sjaarda, Alan; Eichner, Ronald D.
CS John Curtin Sch. Med. Res., Aust. Natl. Univ., Canberra, ACT 2601, Australia
SO Transplantation (1988), 46(1), 120-5
CODEN: TRPLAU; ISSN: 0041-1337
DT Journal
LA English
CC 1-7 (Pharmacology)
AB Gliotoxin, a secondary fungal metabolite, at nanomolar concns., irreversibly inhibits murine T cell proliferation to mitogen. Treatment of **allogeneic** spleen cells with gliotoxin allows their transfer into **sublethally** irradiated recipients without inducing a **graft**-vs.-host (GVH) reaction. Gliotoxin treatment of bone marrow allows the establishment of fully **allogeneic** bone marrow chimeras free of GVH disease. The cytotoxic T cell repertoire against influenza virus in these animals is restricted to both host- and donor-type marrow-derived **hemopoietic cells** (MHC). However, their immune competence is severely compromised by their lack of host MHC-type stimulator cells.
ST gliotoxin bone marrow lymphocyte **transplantation; graft** versus host disease gliotoxin
IT Immunosuppression
(from gliotoxin, in bone marrow **allotransplant, graft** -vs.-host disease prevention in relation to)
IT Lymphocyte
(T-, cytotoxic, gliotoxin inhibition of, in bone marrow **allotransplant, graft**-vs.-host disease prevention in relation to)
IT **Transplant and Transplantation, animal**
(**allo**-, of bone marrow, gliotoxin prevention of **graft** -vs.-host disease in)
IT Bone marrow
(**allotransplant**, gliotoxin prevention of **graft** -vs.-host disease in relation to)
IT **Transplant and Transplantation, animal**
(**graft-vs.-host reaction,**
prevention of, gliotoxin treatment of bone marrow for)
IT 67-99-2, Gliotoxin
RL: BIOL (Biological study)
(**graft**-vs.-host disease prevention by bone marrow treatment with)

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FILE 'HCAPLUS' ENTERED AT 09:25:51 ON 05 NOV 2002
E HEMATOP/CT
E E48+ALL

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L1        16189 S E5
L2        22571 S E5/BI OR E7-13/BI
L3          491 S E6/BI
L4        22386 S E5+NT
L5        28734 S L1-L4
                E STEM CELL/CT
                E E3+ALL
                E E2+ALL
L6         1823 S E2
L7        27151 S E3/BI OR E4/BI
L8        10038 S L5 AND L6,L7
L9        28734 S L5,L8
L10         789 S L9 AND ALLOGEN?
L11         613 S L10 AND TRANSPLANT?
                E TRANSPLANT/CT
L12         494 S E3
                E E4+ALL
                E E2+ALL
L13        7339 S E7-E12
L14       26555 S E6
L15       26623 S E6+NT
                E E35+ALL
L16        5674 S E3
L17        6183 S E3/BI
                E TRANSPLANT/CT
                E E5+ALL
                E E38+ALL
L18        4248 S E2
L19        7055 S E2/BI OR E3/BI
L20         470 S L10 AND L12-L19
L21         616 S L11,L20
L22           8 S L21 AND SUBLETHAL?
L23           0 S L21 AND SUB LETHAL?
L24           4 S L21 AND VETO?
L25          12 S L22,L24
L26        2032 S L9 AND L12-L19
L27        3341 S L9 AND TRANSPLANT?
L28        1575 S L9 AND ?GRAFT?
L29        3616 S L27,L28
L30           8 S L29 AND VETO?
L31          68 S L29 AND SUBLETHAL?
L32          16 S L25,L30
L33           9 S L31 AND L32
L34          16 S L32,L33
L35          59 S L31 NOT L34
L36         628 S L29 AND ALLOGEN?
L37          12 S L36 AND L34
L38           0 S L36 AND L35
L39          16 S L34,L37
L40          59 S L35 NOT L39
                SEL DN AN 8 9 12 14 22 24 37 49
L41           8 S L40 AND E1-E24
L42          24 S L39,L41
L43          54 S (CD33 OR CD 33) AND L29
L44           2 S L43 AND L42
L45          24 S L42,L44
L46          52 S L43 NOT L45
                SEL DN AN 2 3 9 16 17 21 22 26 29 31 42 46
L47          12 S L46 AND E25-E60
L48          36 S L45,L47
                E REISNER Y/AU
L49          59 S E3,E4
L50          32 S L49 AND L1-L48
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                SEL DN AN 1 3-6 10 16 19-23 28 29
L51          14 S L50 AND E1-E36
L52          47 S L48,L51
L53          45 S L49 NOT L52
                SEL DN AN 27
L54           1 S L53 AND E37-E39
L55          48 S L52,L54
L56          48 S L55 AND (?LETHAL? OR ?GRAFT? OR ?TRANSPLANT? OR ?ALLOGEN? OR

     FILE 'HCAPLUS' ENTERED AT 09:54:11 ON 05 NOV 2002
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